PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLIS	HED U	JNDER THE PATENT COOPERATION TREATY (PCT)
1) International Patent Classification ⁶ :		(11) International Publication Number: WO 98/55508
C07K 14/00 A2	A2	(43) International Publication Date: 10 December 1998 (10.12.98)
(21) International Application Number: PCT/JP (22) International Filing Date: 3 June 1998 ((AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT,
(30) Priority Data: 9/144948 3 June 1997 (03.06.97)	:	Published Without international search report and to be republished upon receipt of that report.
(71) Applicants (for all designated States except US): SCHEMICAL RESEARCH CENTER [JP/JF Nishi-Ohnuma 4-chome, Sagamihara-shi, k 229-0012 (JP). PROTEGENE INC. [JP/JP]; Naka-cho, Meguro-ku, Tokyo 153-0065 (JP).	?]; 4– Kanagav	1, va
(72) Inventors; and (75) Inventors/Applicants (for US only): KATO, Seish: 3-46-50, Wakamatsu, Sagamihara-shi, K 229-0014 (JP). SEKINE, Shingo [JP/JP]; 101, 2-8-15, Atago, Ageo-shi, Saitama 362-00; YAMAGUCHI, Tomoko [JP/JP]; 5-13-11, T Katsushika-ku, Tokyo 125-0054 (JP).	Kanagav Remon: 034 (JF	va zu ')
(74) Agents: AOYAMA, Tamotsu et al.; Aoyama & IMP Building, 3-7, Shiromi 1-chome, Chuo-ku, O Osaka 540-0001 (JP).	Partner Saka-sł	rs, ni,
(54) Title: HUMAN PROTEINS HAVING TRANSMEM	IBRAN	E DOMAINS AND DNAS ENCODING THESE PROTEINS
(57) Abstract		
Proteins comprising any of the amino acid sequences of the nucclotide sequences of SEQ ID NOS: 19 to 36 are	of SEC	Q ID NOS: 1 to 18 and DNAs encoding said proteins and comprising any
		•

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LÜ	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TĐ	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	ТJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
ВJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	lL	Israel	. MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of Americ
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	· PL	Poland -		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

1

DESCRIPTION

Human Proteins Having Transmembrane Domains and DNAs Encoding These Proteins

5

FIELD OF THE INVENTION

The present invention relates to human proteins having transmembrane domains and cDNAs encoding these proteins. The membrane proteins of this invention can be used as pharmaceuti10 cals or as antigens for preparing antibodies against said proteins. The cDNAs of the invention can be used as probes for the gene diagnosis and gene sources for the gene therapy. The cDNAs can also be used as gene sources for large-scale production of the membrane proteins encoded by the same. The cells into which the genes encoding the membrane proteins are introduced for expression of such membrane proteins in large amounts can be used for detection of the corresponding ligands, screening of low molecular weight medicines, etc.

20 BACKGROUND OF THE INVENTION

Membrane proteins play important roles as signal receptors, ion channels, transporters, etc. for the material transportation or information transmission mediated by the cell membrane. For instance, they are known to serve as receptors for various cytokines, ion channels for sodium ion, potassium ion, chloride ion, etc., transporters for saccharides and amino acids, and so on. The genes for many of them have been cloned already.

In recent years, it was clarified that the abnormalities

2

of these membrane proteins are related to a number of hitherto cryptogenic diseases. For example, a gene for a membrane protein having 12 transmembrane domains was identified as the gene responsible for cystic fibrosis [Rommens, J. M. et al., 5 Science 245: 1059-1065 (1989)]. It was also clarified that several membrane proteins act as the receptors when a virus infects the cells. For example, HIV-1 was revealed to infect into the cells through the mediation of a membrane protein fusin, a membrane protein on the T-cell membrane, having a CD-4 antigen and 7 transmembrane domains [Feng, Y. et al., Science 272: 872-877 (1996)]. Therefore, the discovery of new membrane proteins is anticipated to lead to the elucidation of the causes of many diseases, and the isolation of new genes coding for the membrane proteins is desired.

Heretofore, owing to the difficulty in their purification, many of membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises transfection of a cDNA library in the animal cells to express the cDNA and detection 20 of the cells expressing the target membrane protein on the membrane by an immunological technique using an antibody or a physiological technique for the change in the membrane permeability. However, this method is applicable only to cloning of a gene for a membrane protein with a known function.

15

25 In general, membrane proteins possess hydrophobic transmembrane domains inside the proteins which are synthesized in the ribosome. Said domains remain in the phospholipid to be trapped in the membrane. Accordingly, the evidence of the cDNA for encoding the membrane protein is provided by determination

3

of the whole base sequence of a full-length cDNA and detection of highly hydrophobic transmembrane domains in the amino acid sequence of the protein encoded by said cDNA.

As a result of the extensive study, there have successful
1 ly been obtained human proteins having transmembrane domains,

particularly comprising any of the amino acid sequences of SEQ

ID NOS: 1 to 18, by cloning cDNAs coding for proteins having

transmembrane domains, particularly comprising any of the

nucleotide sequences of SEQ ID NOS: 19 to 36, from a human

10 full-length cDNA bank. The present invention is based on the

above success.

SUMMARY OF THE INVENTION

A main object of the present invention is to provide novel

human proteins having transmembrane domains, particularly
comprising any of the amino acid sequences of SEQ ID NOS: 1 to

18. Another object of this invention is to provide DNAs coding
for said novel proteins, particularly comprising any of the
nucleotide sequences of SEQ ID NOS: 19 to 36. A further object

of the invention is to provide expression vectors capable of in
vitro translating said DNAs or expressing said DNAs in
eukaryotic cells. A still further object of the invention is
to provide transformed eukaryotic cells capable of expressing
said DNAs to produce said proteins.

In one embodiment, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ ID NOS: 1 to 18 and their fragments.

In another embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.

In a further embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.

10 BRIEF DESCRIPTION OF DRAWINGS

- Figure 1: A figure depicting the structure of the secretory signal sequence detection vector pSSD3.
- Figure 2: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01263.
- Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01299.
 - Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01347.
- Figure 5: A figure depicting the hydrophobicity/hydrophi-20 licity profile of the protein encoded by clone HP01440.
 - Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01526.
 - Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10230.
- 25 Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10389.
 - Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10408.
 - Figure 10: A figure depicting the hydrophobicity/hydro-

5

philicity profile of the protein encoded by clone HP10412.

Figure 11: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10413.

Figure 12: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10415.

Figure 13: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10419.

Figure 14: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10424.

10 Figure 15: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10428.

Figure 16: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10429.

Figure 17: A figure depicting the hydrophobicity/hydro15 philicity profile of the protein encoded by clone HP10432.

Figure 18: A figure depicting the hydrophobicity/hydro-philicity profile of the protein encoded by clone HP10433.

Figure 19: A figure depicting the hydrophobicity/hydro-philicity profile of the protein encoded by clone HP10480.

20

BEST MODE FOR CARRING OUT INVENTION

The proteins of the present invention can be obtained, for example, by isolation from human organs, cell lines, etc., by chemical synthesis on the basis of the amino acid sequences as herein disclosed, or by recombinant DNA technology using the DNA encoding the transmembrane domains of the invention. Among them, adoption of the recombinant DNA technology is preferred. Specifically, each of the proteins may be prepared by in vitro transcription of a vector comprising the cDNA of the invention

PCT/JP98/02445 WO 98/55508

6

to make RNA and in vitro translation using this RNA as a template to accomplish in vitro expression. Also, each of the proteins may be prepared in a large amount by the use of Escherichia coli, Bacillus subtilis, yeasts, animal cells, etc. 5 comprising a suitable expression vector having the DNA encoding such protein.

In the case of producing the protein of the invention by the use of a microorganism such as Escherichia coli, the translation region of the cDNA of the invention is constructed in an expression vector having an origin, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator, etc. that can be replicated in the microorganism and, after transformation of the host cells with said expression vector, the resultant transformant is incubated, whereby the protein 15 encoded by said cDNA can be produced in a large amount in the microorganism. In that case, a protein fragment containing an optional region can be obtained by performing the expression with inserting an initiation codon and a termination codon before and after the optional translation region. Alternatively, a fusion protein with another protein can be expressed. Only a protein portion encoding said cDNA can be obtained by cleavage of said fusion protein with an appropriate protease.

10

For production of the protein of the invention by expression of DNA coding for such protein in eukaryotic cells, the translation region of said cDNA may be recombined into an expression vector for eukaryotic cells having a promoter, a splicing domain, a poly(A) addition site, etc., followed by introduction into eukaryotic cells so that the protein of the invention is produced as a membrane protein on the cell

7

membrane surface. Examples of the expression vector are pKA1, pED6_dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, etc. As the eukaryotic cells, there are exemplified mammalian animal culture cells (e.g. simian kidney 5 cells COS7, chinese hamster ovary cells CHO), budding yeasts, Schizosaccharomyces pombe, silkworm cells, Xenopus laevis egg cells, etc., but any other eukaryotic cells may also be used insofar as the protein of the invention can be expressed on the membrane surface. In order to introduce the expression vector into eukaryotic cells, there may be adopted any conventional procedure such as electroporation, calcium phosphate method, liposome method or DEAE dextran method.

10

25

The proteins of the present invention include peptide fragments (5 or more amino acid residues) containing any 15 partial amino acid sequence of the amino acid sequences of SEQ ID NOS: 1 to 18. These fragments can be used as antigens for preparation of the antibodies. Also, the proteins of the invention that have signal sequences appear in the form of maturation proteins on the cell surface, after the signal 20 sequences are removed. Therefore, these maturation proteins shall come within the scope of the present invention. The Nterminal amino acid sequences of the maturation proteins can be easily identified by using the method for the cleavage-site determination in a signal sequence [Japan Patent Kokai No. 187100/96]. Further, many membrane proteins are subjected to the processing on the cell surface to be converted to the secretor forms. These secretor proteins or peptides shall come within the scope of the present invention. When glycosylation sites are present in the amino acid sequences, expression in

8

appropriate animal cells affords glycosylated proteins. Therefore, these glycosylated proteins or peptides also shall come within the scope of the invention.

The DNAs of the invention include all DNAs encoding the above-mentioned proteins. Said DNAs can be obtained using the method by chemical synthesis, the method by cDNA cloning, and so on.

Each of the cDNAs of the invention can be cloned from, for example, the cDNA libraries of the human cell origin. The cDNA is synthesized using as a template a poly(A)⁺ RNA extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the culture cells. The cDNA can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)] as illustrated in Examples in order to obtain a full-length clone in an effective manner.

The primary selection of a cDNA encoding a human protein having transmembrane domains is performed by the sequencing of a partial base sequence of the cDNA clone selected at random from the cDNA libraries, sequencing of the amino acid sequence encoded by the base sequence, and recognition of the presence or absence of hydrophobic site(s) in the resulting N-terminal amino acid sequence region. Next, the secondary selection is carried out by determination of the whole base sequence by the sequencing and the protein expression by the in vitro translation. The ascertainment of the cDNA of the present

20

9

invention for encoding the protein having the secretory signal sequence is performed by using the signal sequence detection method [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. In other words, the ascertainment for the coding portion of the inserted cDNA fragment to function as a signal sequence is provided by fusing a cDNA fragment encoding the N-terminus of the target protein with a cDNA encoding the protease domain of urokinase and then expressing the resulting cDNA in COS7 cells to detect the urokinase activity in the cell culture medium. On the other hand, the N-terminal region is judged to remain in the membrane in the case where the urokinase activity is not detected in the cell culture medium.

The cDNAs of the invention are characterized by containing any of the nucleotide sequences of SEQ ID NOS: 19 to 36 or any of the nucleotide sequences of SEQ ID NOS: 37 to 54. Table 1 summarizes the clone number (HP number), the cells affording the cDNA, the total nucleotide number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

10

Table 1

5	Sequence Number	HP Number	Cells	Number of Nucleotides	Number of Amino Acid Residues
10	1, 19, 37	HP01263	Liver	1502	382
10	2, 20, 38	HP01299	Liver	1349	317
	3, 21, 39	HP01347	Liver	1643	296
15	4, 22, 40	HP01440	Stomach cancer	729	197
	5, 23, 41	HP01526	Stomach cancer	1322	221
20	6, 24, 42	HP10230	Stomach cancer	3045	251
20	7, 25, 43	HP10389	KB	653	106
	8, 26, 44	HP10408	Stomach cancer	439	78
25	9, 27, 45	HP10412	Stomach cancer	1131	314
	10, 28, 46	HP10413	Stomach cancer	1875	195
30	11, 29, 47	HP10415	Stomach cancer	1563	462
30	12, 30, 48	HP10419	Stomach cancer	2030	247
	13, 31, 49	HP10424	Stomach cancer	493	113
35	14, 32, 50	HP10428	KB .	2044	365
	15, 33, 51	HP10429 ·	Stomach cancer	1043	226
40	16, 34, 52	HP10432	Liver	972	129
	17, 35, 53	HP10433	Liver	695	163
	18, 36, 54	HP10480	Stomach cancer	1914	193

45

Hereupon, the same clone as any of the cDNAs of the invention can be easily obtained by screening of the cDNA libraries constructed from the cell line or the human tissues employed in the invention, by the use of an oligonucleotide probe synthesized on the basis of the corresponding cDNA nucleotide sequence of SEQ ID NOS: 37 to 54.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Therefore, any cDNA that is subjected to insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides

11

in SEQ ID NOS: 37 to 54 shall come within the scope of the invention.

In a similar manner, any protein that is produced by these modifications comprising insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides shall come within the scope of the present invention, as far as said protein possesses the activity of the corresponding protein having the amino acid sequence of SEQ ID NOS: 1 to 18.

The cDNAs of the invention include cDNA fragments (more than 10 bp) containing any partial nucleotide sequence of the nucleotide sequence of SEQ ID NOS: 19 to 36 or of the nucleotide sequence of SEQ ID NOS: 37 to 54. Also, DNA fragments consisting of a sense chain and an anti-sense chain shall come within this scope. These DNA fragments can be used as the probes for the gene diagnosis.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate

12

genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

5 Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave 10 the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that 15 have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified 20 genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 Bl, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to 25 the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through

WO 98/55508

13

PCT/JP98/02445

insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 5 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 10 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are Such organisms are useful for the development of mammals. non-human models for the study of disorders involving the 15 corresponding gene(s), and for the development of assay systems for the identi fication of molecules that interact with the protein product(s) of the corresponding gene(s).

Where the protein of the present invention membrane-bound (e.g., is a receptor), the present invention 20 also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be 25 identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at

14

least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined 5 by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, 10 most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the 25 disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences

15

complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably 5 highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example,

Table 2

Stringency	Polynucleotide	Hybrid	Hybridization Temperature	Wash
Condition	Hybrid	Length	and Buffer [†]	Temperature
		(bp) [‡]		and Buffer [†]
Α	DNA : DNA	≥50	65℃; 1×SSC -or-	65°C; 0.3×SSC
			42℃; 1×SSC,50% formamide	
B	DNA : DNA	<50	T_B^* ; 1×SSC	T _B *; 1×SSC
С	DNA : RNA	≥50	67°C; 1×SSC -or-	67℃; 0.3×SSC
			45°C; 1×SSC,50% formamide	
D	DNA: RNA	<50	T _D *; 1×SSC	T _D *; 1×SSC
Е	RNA: RNA	≥50	70℃; 1×SSC -or-	70°C; 0.3×SSC
			50℃; 1×SSC,50% formamide	
F	RNA: RNA	<50	T _F *; 1×SSC	T _F *; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or-	65℃; 1×SSC
			42°C; 4×SSC,50% formamide	<u> </u>
H	DNA : DNA	<50	T _H *; 4×SSC	T _H *; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or-	67°C; 1×SSC
			45°C; 4×SSC,50% formamide	
J	DNA : RNA	<50	T _J *; 4×SSC	T _J *; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or-	67°C; 1×SSC
			50°C; 4×SSC,50% formamide	·
L	RNA: RNA	<50	T _L *; 2×SSC	T _L *; 2×SSC
M	DNA : DNA	≥50	50°C; 4×SSC -or-	50°C; 2×SSC
			40°C; 6×SSC,50% formamide	,
N	DNA : DNA	<50	T _N *; 6×SSC	T _N *; 6×SSC
0	DNA : RNA	≥50	55°C; 4×SSC -or-	55°C; 2×SSC
			42°C; 6×SSC,50% formamide	
P	DNA : RNA	<50	T _P *; 6×SSC	T _P *; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or-	60°C; 2×SSC
•			45°C; 6×SSC,50% formamide	
R	RNA : RNA	<50	T _R *; 4×SSC	T _R *; 4×SSC

- ‡: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.
- †: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH₂PO₄, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.
- * T_B T_R : The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m (°C)=2(#of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m (°C)=81.5 + 16.6(log₁₀[Na⁺]) + 0.41 (%G+C) (600/N), where N is the number of bases in the hybrid, and [Na⁺] is the concentration of sodium ions in the hybridization buffer ([Na⁺] for 1×SSC=0.165M).

17

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory

- 5 Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.
- length that is at least 25%(more

 preferably at least 50%, and most preferably at least 75%) of
 the length of the polynucleotide of
 the present invention to which it hybridizes, and has at least

 60% sequence identity (more
 preferably, at least 75% identity; most preferably at least 90%
 or 95% identity) with the
 polynucleotide of the present invention to which it hybridizes,
 where sequence identity is
- 20 determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

25 EXAMPLE

The present invention is embodied in more detail by the following examples, but this embodiment is not intended to restrict the present invention. The basic operations and the enzyme reactions with regard to the DNA recombination are

18

carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo Co., Ltd. The manufacturer's instructions were used for the buffer compositions as well as for the reaction conditions, in each of the enzyme reactions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

10 (1) Preparation of Poly(A) + RNA

The epidermoid carcinoma cell line KB (ATCC CRL 17), tissues of stomach cancer delivered by the operation, and liver were used for human cells to extract mRNAs. The cell line was cultured by a conventional procedure.

15 After about 1 g of human tissues was homogenized in 20 ml of a 5.5 M guanidinium thiocyanate solution, total mRNAs were prepared in accordance with the literature [Okayama, H. et al., "Methods in Enzymology" Vol. 164, Academic Press, 1987]. These mRNAs were subjected to chromatography using an oligo(dT)-20 cellulose column washed with 20 mM Tris-hydrochloric acid buffer solution (pH 7.6), 0.5 M NaCl, and 1 mM EDTA to obtain a poly(A)⁺ RNA in accordance with the above-mentioned literature.

(2) Construction of cDNA Library

To a solution of 10 μg of the above-mentioned poly(A)⁺ RNA in 100 mM Tris-hydrochloric acid buffer solution (pH 8) was added one unit of an RNase-free, bacterium-origin alkaline phosphatase and the resulting solution was allowed to react at 37°C for one hour. After the reaction solution underwent the

WO 98/55508

19

PCT/JP98/02445

phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 50 mM sodium acetate (pH 6), 1 mM EDTA, 0.1% 2-mercaptoethanol, and 0.01% Triton X-100. Thereto was added one unit of a tobacco-origin pyrophosphatase (Epicenter Technologies) and the resulting solution at a total volume of 100 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a decapped poly(A)[†] RNA solution.

To a solution of the decapped poly(A)⁺ RNA and 3 nmol of a DNA-RNA chimeric oligonucleotide (5'-dG-dG-dG-dG-dA-dA-dT-dT-dC-dG-dA-G-G-A-3') in a mixed aqueous solution of 50 mM Trishydrochloric acid buffer solution (pH 7.5), 0.5 mM ATP, 5 mM MgCl₂, 10 mM 2-mercaptoethanol, and 25% polyethylene glycol were added 50 units of T4 RNA ligase and the resulting solution at a total volume of 30 μ l was allowed to react at 20°C for 12 hours. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a chimeric oligo-capped poly(A)⁺ RNA.

After the vector pKA1 developed by the present inventors (Japanese Patent Kokai Publication No. 1992-117292) was digested with KpnI, an about 60-dT tail was inserted by a terminal transferase. This product was digested with EcoRV to remove the dT tail at one side and the resulting molecule was used as a vectorial primer.

After 6 μ g of the previously-prepared chimeric oligo-capped poly(A)[†] RNA was annealed with 1.2 μ g of the vectorial

primer, the product was dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 8.3), 75 mM KCl, 3 mM $MgCl_2$, 10 mM dithiothreitol, and 1.25 mM dNTP (dATP + dCTP + dGTP + dTTP), mixed with 200 units of a reverse transferase 5 (GIBCO-BRL), and the resulting solution at a total volume of 20 µl was allowed to react at 42°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in a mixed solution of 50 mM Tris-hydrochloric acid 10 buffer solution (pH 7.5), 100 mM NaCl, 10 mM MgCl $_2$, and 1 mM dithiothreitol. Thereto were added 100 units of EcoRI and the resulting solution at a total volume of 20 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol 15 precipitation, the obtained pellets were dissolved in a mixed solution of 20 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM KCl, 4 mM MgCl₂, 10 mM $(NH_4)_2SO_4$, and 50 $\mu g/ml$ bovine serum albumin. Thereto were added 60 units of Escherichia coli DNA ligase and the resulting solution was 20 allowed to react at 16°C for 16 hours. To the reaction solution were added 2 µl of 2 mM dNTP, 4 units of Escherichia coli DNA polymerase I, and 0.1 unit of Escherichia coli DNase H and the resulting solution was allowed to react at 12°C for one hour and then at 22°C for one hour.

Next, the cDNA-synthesis reaction solution was used to transform Escherichia coli DH12S (GIBCO-BRL). The transformation was carried out by the electroporation method. A portion of the transformant was inoculated on a 2xYT agar culture medium containing 100 µg/ml ampicillin, which was

21

incubated at 37°C overnight. A colony grown on the culture medium was randomly picked up and inoculated on 2 ml of the 2xYT culture medium containing 100 $\mu g/ml$ ampicillin, which was incubated at 37°C overnight. The culture medium was centrifuged 5 to separate the cells, from which a plasmid DNA was prepared by the alkaline lysis method. After the plasmid DNA was doubledigested with EcoRI and NotI, the product was subjected to 0.8% agarose gel electrophoresis to determine the size of the cDNA insert. In addition, by the use of the obtained plasmid as a 10 template, the sequence reaction using M13 universal primer labeled with a fluorescent dye and Taq polymerase (a kit of Applied Biosystems Inc.) was carried out and the product was analyzed by a fluorescent DNA-sequencer (Applied Biosystems Inc.) to determine the base sequence of the cDNA 5'-terminal of 15 about 400 bp. The sequence data were filed as a homo-protein cDNA bank data base.

(3) Selection of cDNAs Encoding Proteins Having
Transmembrane Domains

The base sequence registered in the homo-protein cDNA bank

20 data base was converted to three frames of amino acid sequences
and the presence or absence of an open reading frame (ORF)
beginning from the initiation codon. Then, the selection was
made for the presence of a signal sequence that is
characteristic to a secretory protein at the N-terminal of the

25 portion encoded by ORF. These clones were sequenced from the
both 5' and 3' directions by using the deletion method to
determine the sequence of the whole base sequence. The
hydrophobicity/hydrophilicity profiles were obtained for
proteins encoded by ORF by the Kyte-Doolittle method [Kyte, J.

WO 98/55508

22

PCT/JP98/02445

& Doolittle, R. F., J. Mol. Bio. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. In the case in which there is a hydrophobic region of putative transmembrane domain(s) in the amino acid sequence of an encoded protein, this protein was considered as a membrane protein.

(4) Construction of Secretory Signal Detection Vector pSSD3

One microgram of pSSD1 carrying the SV40 promoter and a cDNA encoding the protease domain of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)] was digested with 5 units of BglII and 5 units of EcoRV. Then, after dephosphorylation at the 5' terminal by the CIP treatment, a DNA fragment of about 4.2 kbp was purified by cutting off from the gel of agarose gel electrophoresis.

Two oligo DNA linkers, L1 (5'-GATCCCGGGTCACGTGGGAT-3') and L2 (5'-ATCCCACGTGACCCGG-3'), were synthesized phosphorylated by T4 polynucleotide kinase. After annealing of the both linkers, followed by ligation with the previously-20 prepared pSSD1 fragment by T4 DNA ligase, Escherichia coli JM109 was transformed. A plasmid pSSD3 was prepared from the transformant and the objective recombinant was confirmed by the determination of the base sequence of the linker-inserted fragment. Figure 1 illustrates the structure of the thus-25 obtained plasmid. The present plasmid vector carries three types of blunt-end formation restriction enzyme sites, SmaI, PmaCI, and EcoRV. Since these cleavage sites are positioned in succession at an interval of 7 bp, selection of an appropriate site in combination of three types of frames for the inserting

cDNA allows to construct a vector expressing a fusion protein.

23

(5) Functional Verification of Secretory Signal Sequence Whether the N-terminal hydrophobic region in the secretory protein clone candidate obtained in the above-mentioned steps functions as the secretory signal sequence was verified by the method described in the literature [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. First, the plasmid containing the target cDNA was cleaved at an appropriate restriction enzyme site that existed at the downstream of the portion 10 expected for encoding the secretory signal sequence. In the case in which this restriction enzyme site was a protruding terminus, the site was blunt-ended by the Klenow treatment or treatment with the munq-bean nuclease. Digestion with HindIII was further carried out and a DNA fragment containing the SV40 15 promoter and a cDNA encoding the secretory sequence at the downstream of the promoter was separated by agarose gel electrophoresis. This fragment was inserted between the pSSD3 HindIII site and a restriction enzyme site selected so as to match with the urokinase-coding frame, thereby constructing a 20 vector expressing a fusion protein of the secretory signal portion of the target cDNA and the urokinase protease domain.

After Escherichia coli (host: JM109) bearing the fusionprotein expression vector was incubated at 37°C for 2 hours in
2 ml of the 2xYT culture medium containing 100 μg/ml
25 ampicillin, the helper phage M13KO7 (50 μl) was added and the
incubation was continued at 37°C overnight. A supernatant
separated by centrifugation underwent precipitation with
polyethylene glycol to obtain single-stranded phage particles.
These particles were suspended in 100 μl of 1 mM Tris-0.1 mM

24

EDTA, pH 8 (TE). Also, there was used as a control a suspension of single-stranded particles prepared in the same manner from the vector pLA1-UPA containing pSSD3 and a full-length cDNA of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)].

5

simian-kidney-origin culture cells, COS7, The incubated at 37°C in the presence of 5% ${\rm CO_2}$ in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% bovine fetus albumin. Into a 6-well plate (Nunc Inc., 3 cm in the well 10 diameter) were inoculated 1 \times 10⁵ COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO2. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) 15 (TDMEM). To the cells were added 1 μ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3 μ l of TRANSFECTAMTM (IBF Inc.) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO2. After the sample solution was removed, the cell surface was washed 20 with TDMEM, 2 ml per well of DMEM containing 10% bovine fetus albumin was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO2.

To 10 ml of 50 mM phosphate buffer solution (pH 7.4) containing 2% bovine fibrinogen (Miles Inc.), 0.5% agarose, and 1 mM potassium chloride were added 10 units of human thrombin (Mochida Pharmaceutical Co., Ltd.) and the resulting mixture was solidified in a plate of 9 cm in diameter to prepare a fibrin plate. Ten microliters of the culture supernatant of the

10

20

WO 98/55508 PCT/JP98/02445

transfected COS7 cells were spotted on the fibrin plate, which was incubated at 37°C for 15 hours. The diameter of the thusobtained clear circle was taken as an index for the urokinase activity. In the case in which a cDNA fragment codes for the amino acid sequence that functions as a secretory signal sequence, a fusion protein is secreted to form a clear circle by its urokinase activity. Therefore, in the case in which a clear circle is not formed, the fusion protein remains as trapped in the membrane and the cDNA fragment is considered to code for a transmembrane domain.

(6) Protein Synthesis by In Vitro Translation

The plasmid vector carrying the cDNA of the present invention was utilized for the transcription/translation by the T_NT rabbit reticulocyte lysate kit (Promega Biotec). In this case, [35S]methionine was added and the expression product was labeled with the radioisotope. All reactions were carried out by following the protocols attached to the kit. Two micrograms of the plasmid was allowed to react at 30°C for 90 minutes in total 25 ml of a reaction solution containing 12.5 µl of the T_NT rabbit reticulocyte lysate, 0.5 μ l of the buffer solution (attached to the kit), 2 µl of an amino acid mixture (methionine-free), 2 μ l (0.37 MBq/ μ l) of [35 S]methionine (Amersham Corporation), 0.5 μl of T7 RNA polymerase, and 20 U of RNasin. To 3 μ l of the reaction solution was added 2 μ l of an SDS sampling buffer (125 mM Tris-hydrochloric acid suffer solution, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting solution was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of

26

the translation product was determined by carrying out the autoradiography.

(7) Expression in COS7

Escherichia coli bearing a vector expressing the protein of the invention was infected with helper phage M13KO7, and single-stranded phage particles were obtained according to the method as stated above. Using the thus obtained phages, each expression vecotr was introduced into simian-kidney-origin culture cells COS7 in the manner as stated above. After incubation at 37 °C for 2 days in the presence of 5 % CO₂, further incubation was carried out in a medium containing [35S]cysteine or [35S]methionine for 1 hour. The cells were collected, dissolved and then subjected to SDS-PAGE whereby a band corresponding to the expression product of each protein which is not present in COS7 cells was revealed. In Table 3, the molecular weight of each expression product is shown.

Table 3

HP Number	Supernatant of culture	Membrane fraction
	(kDa)	(kDa)
HP01263	50	-
HP01299	-	30
HP01526	~	22
HP10230		24
HP10408	<u>-</u>	7
HP10415	-	45
HP10424	_	14
HP10429	-	27
HP10432	- ·	17
HP10480	_	22 .

27

(8) Clone Examples

<HP01263> (Sequence Number 1, 19, 37)

Determination of the whole base sequence for the cDNA insert of clone HP01263 obtained from the human liver cDNA 5 libraries revealed the structure consisting of a 5'-nontranslation region of 36 bp, an ORF of 1149 bp, and a 3'-nontranslation region of 316 bp. The ORF codes for a protein consisting of 382 amino acid residues with one transmembrane domain at the N-terminal. Figure 2 depicts the hydrophobicity 10 /hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in formation of a translation product of 42 kDa, which is almost consistent with the molecular weight of 42,054 as predicted from the ORF. On expression in COS cells, an expression 15 product of about 50 kDa was observed in the culture supernatant. Therefore, said protein can be understood to be a secreted protein. Application of the rule (-3, -1) as a method for anticipation of a cutting site in a secretion signal sequence suggested that the mature protein would start from 20 methionine at 19 position.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human α -2-HS-glycoprotein (SWISS-PROT Accession No. P02765). Table 4 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human α -2-HS-glycoprotein (GP). represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the

protein of the present invention. The both proteins possessed a homology of 25.5%. The cysteine position is reserved and this region is analogous to that in cystatins (thiol proteinase inhibitors). There are observed other analogy with histidine-rich glycoprotein (P04196, 30.9%/194 amino acid residues), kininogen (P01045, 24.1%/261 amino acid residues), tyrosine kinase inhibitor (A32827, 24.4%/291 amino acid residues), and so on.

Table 4

10 HP MGLLLPLALCILVLCCGAMSPPQLALNPSALLSR--GCNDSDVLAVAGFALRDINKDRKD GP MKSLVLLLCLAQLWGCHSAPHGPGLIYRQPNCDDPETEEAALVAIDYINQNLPW HP GYVLRLNRVNDAQEYRRGGLGSLFYLTLDVLETDCHVLRKKAWQDCGMRIFFE-SVYGQC 15 GYKHTLNQIDEVKVWPQQPSGELFEIEIDTLETTCHVLDPTPVARCSVRQLKEHAVEGDC HP K-AIFYMNNPSRVLYLAAYNCTLRPVSKKKIYMTCPDCPSSIPTDSSNHQVLEAATESLA GP DFQLLKLDGKFSVVY---AKCDSSPDSAEDVRKVCQDCPLLAPLN--DTRVVHAAKAALA 20 HP KYNNENTSKQYSLFKVTRASSQWVVGPSYFVEYLIKESPC---TKSQASSCSLQSSDSVP .*..*... * ...** . ** .**. * GP AFNAQNNGSNFQLEEISRAQLV-PLPPSTYVEFTVSGTDCVAKEATEAAKCNLLAEKQY-HP VGLCKGSLTRTHWEKFVSVTCDFFESQAPATGSENSAVNQK-PTNLPKVEESQQKNTPPT *.**..*. *.*. *..*. *..*. ** 25 GP -GFCKATLSEKLGGAEVAVTCTVFQTQPVTSQPQPEGANEAVPTPVVDPDAPPSPPLGAP HP DSPSKAGPRGSVQYLPDLDDKNSQEKGPQEAFPVHLDLTTNPQGETLDISFLFLEPMEEK . *. ..*..* GP GLPPAGSPPDSHVLLAAPPGHQLHRAHYDLRHTFMGVVSLGSPSGEVSHPRKTRTVVQPS HP LVVLPFPKEKARTAECPGPAQNASPLVLPP 30 GP VGAAAGPVVPPCPGRIRHFKV

WO 98/55508

PCT/JP98/02445

29

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H57204), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention. Hereupon, most of ESTs matching with the present cDNA are available from liver cDNA libraries, whereby the present clone is considered to be expressed specifically in the liver.

The present protein, because of being a type-II membrane protein, is considered to exert its function as a receptor on the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. The present protein, because of bearing a cystatin-like domain, is considered to possess a proteinase-inhibitor activity as well as many physiological activities in the same manner as for other members of this family. In addition, the present protein, because of being expressed specifically in liver cells, is considered to play a significant role for maintaining the liver function.

<HP01299> (Sequence Number 2, 20, 38)

Determination of the whole base sequence for the cDNA insert of clone HP01299 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 110 bp, an ORF of 954 bp, and a 3'-non-translation region of 285 bp. The ORF codes for a protein consisting of 317 amino acid residues with two or more transmembrane domains. Figure 3 depicts the hydrophobicity/hydrophilicity profile of the present protein

30

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 32 kDa that was almost consistent with the molecular weight of 35,965 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the rat retinol dehydrogenase (NBRF Accession No. A55884). Table 5 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the rat retinol dehydrogenase (RN). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 65.3% among the entire regions.

Table 5

	HP	MWLYLAAFVGLYYLLHWYRERQVVSHLQDKYVFITGCDSGFGNLLARQLDARGLRVLAAC
5		**** *.**. *****.******************
	RN	${\tt MWLYLLALVGLWNLLRLFRERKVVSHLQDKYVFITGCDSGFGNLLARQLDRRGMRVLAAC}$
	HР	LTEKGAEQLRGQTSDRLETVTLDVTKMESIAAATQWVKEHVGDRGLWGLVNNAGILTPIT

	RN	LTEKGAEQLRSKTSDRLETVILDVTKTESIVAATQWVKERVGNRGLWGLVNNAGISVPVG
10	HP	LCEWLNTEDSMNMLKVNLIGVIQVTLSMLPLVRRARGRIVNVSSILGRVAFFVGGYCVSK
		****.**********************
	RN	PNEWMRKKDFASVLDVNLLGVIEVTLNMLPLVRKARGRVVNIASTMGRMSLVGGGYCISK
	HP	YGVEAFSDILRREIQHFGVKISIVEPGYFRTGMTNMTQSLERMKQSWKEAPKHIKETYGQ
		******* ******** *.*****. ***.**
15	RN	YGVEAFSDSLRRELTYFGVKVAIIEPGGFKTNVTNMERLSDNLKKLWDQTTEEVKEIYGE
	HP	QYFDALYNIMKEGLLNCSTNLNLVTDCMEHALTSVHPRTRYSAGWDAKFFFIPLSYLPTS
		* * ***.******** **********
	RN	KFQDSYMKAMESLVNTCSGDLSLVTDCMEHALTSCHPRTRYSPGWDAKFFYLPMSYLPTF
	HP	LADYILTRSWPKPAQAV
20		*.* ***.*.
	RN	LSDAVIHWGSVKPARAL

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. R35197), but any of them was shorter than the present cDNA and did not contain the initiation codon.

The rat retinol dehydrogenase has been found as a 30 microsomal membrane protein participating in the retinoic acid

WO 98/55508

biosynthesis in the liver [Chai, X. et al., J. Biol. Chem. 270: 28408-28412 (1995)]. Accordingly, its homologue, the protein of the present invention, is considered to possess a similar function and can be utilized for diagnosis and treatment of diseases caused by the abnormality of this protein.

32

PCT/JP98/02445

<HP01347> (Sequence Number 3, 21, 39)

Determination of the whole base sequence for the cDNA insert of clone HP01347 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-10 translation region of 24 bp, an ORF of 891 bp, and a 3'-nontranslation region of 728 bp. The ORF codes for a protein consisting of 296 amino acid residues with one transmembrane domain at the N-terminal. Figure depicts hydrophobicity/hydrophilicity profile of the present protein 15 obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified and the urokinase activity was detected on the membrane surface, upon transduction into the COS7 cells of an expression vector in which a HindIII-SacI fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 73 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein is considered to be a type-II membrane protein. The in vitro 25 translation resulted in the formation of a translation product of 33 kDa that was almost consistent with the molecular weight of 33,527 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was

33

analogous to the human HIV envelope glycoprotein gp120-binding C-type lectin (GenBank Accession No. M98457). Table 6 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human HIV envelope glycoprotein gp120-binding C-type lectin (CL). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 85.6% among 284 amino acid residues. There is observed at the downstream of the transmembrane domain a sequence with seven repetition of Ile-Tyr-Gln-Xaa-Leu-Thr-Xaa-Leu-Lys-Ala-Ala-Val-Gly-Glu-Leu-Xaa-Xaa-Xaa-Ser-Lys-Xaa-Gln-Xaa.

15

34

Table 6

HP MSDSKEPRVQQLGLL-------GCLGHGALVLQLLSFMLLAGVLVAI ****** ***** ***** CL MSDSKEPRLQQLGLLEEEQLRGLGFRQTRGYKSLAGCLGHGPLVLQLLSFTLLAG----L HP LVQVSKVPSSLSQEQSEQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE ************ CL LVQVSKVPSSISQEQSRQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRL 10 ************************ CL KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTWLKAAVGELPEKSKMQEIYQELTRL HP KAAVGELPEKSKLQEIYQELTELKAAVGELPEKSKLQEIYQELTQLKAAVGELPDQSKQQ CL KAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQ 15 HP QIYQELTDLKTAFERLCRHCPKDWTFFQGNCYFMSNSQRNWHDSVTACQEVRAQLVVIKT CL EIYQELTQLKAAVERLCHPCFWEWTFFQGNCYFMSNSQRNWHDSITACKEVGAQLVVIKS HP AEEQLPAVLEQWRTQQ *. *... **** 20 CL AEEQNFLQLQSSRSNRFTWMGLSDLNQEGTWQWVDGSPLLPSFKQYWNRGEPNNVGEEDC

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H90360), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The present protein, because of being a type-II membrane 30 protein, is considered to exert its function as a receptor on

WO 98/55508

the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. Hereupon, the human HIV envelope glycoprotein gpl20-binding C-type lectin that is highly 5 homologous with the present protein has been found as a CD4independent HIV receptor [Curtis, B. M. et al., Proc. Natl. Acad. Sci. USA 89: 8356-8360 (1992)].

35

PCT/JP98/02445

<HP01440> (Sequence Number 4, 22, 40)

Determination of the whole base sequence for the cDNA insert of clone HP01440 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 37 bp, an ORF of 594 bp, and a 3'-nontranslation region of 98 bp. The ORF codes for a protein consisting of 197 amino acid residues with four transmembrane 15 domains. Figure 5 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 20,822 predicted from the ORF.

20 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human tumor-associated antigen L6 (SWISS-PROT Accession No. P30408). Table 7 indicates the comparison of the amino acid sequences between the human protein of the present 25 invention (HP) and the human tumor-associated antigen L6 (L6). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

36

a homology of 47.0% among the entire regions.

Table 7

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. T55097), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

The human tumor-associated antigen L6 is a member of a membrane antigen TM4 superfamily proteins which are expressed in large quantities on the surface of human tumor cells [Marken, J. S. et al., Proc. Natl. Acad. Sci. USA 89: 3503-3507 (1992)]. Since these membrane antigens are expressed specifically on some specified cells or cancer cells,

WO 98/55508

20

PCT/JP98/02445

antibodies against these antigens, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are 5 expressed are applicable for detection of the corresponding ligands and so on.

37

<HP01526> (Sequence Number 5, 23, 41)

Determination of the whole base sequence for the cDNA insert of clone HP01526 obtained from the human stomach cancer 10 cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 83 bp, an ORF of 666 bp, and a 3'-nontranslation region of 573 bp. The ORF codes for a protein consisting of 221 amino acid residues with a hydrophobic region of putative six transmembrane domains. Figure 6 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was almost consistent with the molecular weight of 25,030 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the mouse interstitial cell protein (GenBank Accession No. X96618). Table 8 indicates the comparison of the amino acid sequences between the human protein of the present 25 invention (HP) and the mouse interstitial cell protein (MM). represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

38

a homology of 79.6% among the entire regions.

Table 8

Furthermore, the search of GenBank using the base sequence 20 of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. H02682), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

The mouse interstitial cell protein has been cloned as a membrane protein that is expressed with highly increasing in interstitial cells stimulated by a cytokine [Tagoh, H. et al., Biochem. Biophys. Res. Commun. 221: 744-749 (1996)]. Since these membrane proteins are expressed specifically on some specified cells and cancer cells, antibodies against these

39

proteins, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are expressed are applicable for detection of the corresponding ligands and so on.

<HP10230> (Sequence Number 6, 24, 42)

Determination of the whole base sequence for the cDNA insert of clone HP10230 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-10 translation region of 190 bp, an ORF of 756 bp, and a 3'-nontranslation region of 2099 bp. The ORF codes for a protein consisting of 251 amino acid residues with at least one transmembrane domain. Figure 7 depicts hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 30 kDa that was almost consistent with the molecular weight of 28,800 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein F25D7.1 (GenBank Accession No. Z78418). Table 9 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein F25D7.1 (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 49.8% among the entire regions.

Table 9

HS MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFL-WPEAFLYRFQIWRPITAT 5 CE MDLENFLLGIPIVTRYWFLASTIIPLLGRFGFINVQWMFLQW-DLVVNKFQFWRPLTAL HS FYFPVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNW-ICIVITGLAMDM CE IYYPVTPQTGFHWLMMCYFLYNYSKALESETYRGRSADYLFMLIFNWFFCSGLC-MALDI HS QLLMIPLIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIGGSVINELIGNL 10 .*. *...***** *.*.* ****** ** * *****. *** .. *. .***.* * CE YFLLEPMVISVLYVWCQVNKDTIVSFWFGMRFPARYLPWVLWGFNAVLRGGGTNELVGIL HS VGHLYFFLMFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGG *** ***. ..** . * ...***.* .*. **. * CE VGHAYFFVALKYPDEYGV-DLISTPEFLHRLIPDEDGGIHG---QDGNIRGARQQPRG--15 HS RHNW--GQGFRLGDQ * * * * *** CE -HQWPGGVGARLGGN

20 Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. W01493), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10389> (Sequence Number 7, 25, 43)

Determination of the whole base sequence for the cDNA insert of clone HP10389 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 62 bp, an ORF of

PCT/JP98/02445

321 bp, and a 3'-non-translation region of 270 bp. The ORF codes for a protein consisting of 106 amino acid residues with a hydrophobic region of putative two transmembrane domains. Figure 8 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 12 kDa that was almost consistent with the molecular weight of 11,528 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any of known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H70816), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10408> (Sequence Number 8, 26, 44)

20

Determination of the whole base sequence for the cDNA insert of clone HP10408 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 74 bp, an ORF of 237 bp, and a 3'-non-translation region of 128 bp. The ORF codes for a protein consisting of 78 amino acid residues with a putative signal sequence at the N-terminal as well as a sequence of one putative interior transmembrane domain. Figure 9 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified

42

upon transduction into the COS7 cells of an expression vector in which a HindIII-BglII fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 70 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 9 kDa that was almost consistent with the molecular weight of 8,396 predicted from the ORF.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T94049), but they were shorter than the present cDNA and any molecule containing the initiation codon was not identified.

15 <HP10412> (Sequence Number 9, 27, 45)

20

25

Determination of the whole base sequence for the cDNA insert of clone HP10412 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 55 bp, an ORF of 945 bp, and a 3'-nontranslation region of 131 bp. The ORF codes for a protein consisting of 314 amino acid residues with one transmembrane N-terminal. the Figure 10 depicts domain at the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-ApaI fragment (treated with mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 65

43

amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 44 kDa that was somewhat larger than the molecular weight of 35,610 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein of 28.5 kDa (SWISS-PROT Accession No. P34623). Table 10 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein of 28.5 kDa (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 42.8% in the C-terminal region of 243 amino acid residues.

Table 10

	HP	${\tt MVAPVWYLVAAALLVGFILFLTRSRGRAASAGQEPLHNEELAGAGRVAQPGPLEPEEPRA}$
5	нР	GGRPRRRDLGSRLQAQRRAQRVAWAEADENEEEAVILAQEEEGVEKPAETHLSGKIG
		* * * * * * . *
	CE	MRRNARRRVNRDEQEDGFVNHMMNDGEDVEDLDGGAEQFEYDEDGKKIG
	HP	${\tt AKKLRKLEEKQARKAQREAEEAEREERKRLESQREAEWKKEEERLRLEEEQKEEEErK}$
		.* *** ** * ****** ** * **** . **.**
10	CE	KRKAAKLQAKEEKRQMREYEVREREERKRREEEREKKRDEERAKEEADEKAEEERLRK
	HP	AREEQAQREHEEYLKLKEAFVVEEEGVGETMTEEQSQSFLTEFINYIKQSKVVLLEDLAS
		.******** .***
	CE	EREEKERKEHEEYLAMKASFAIEEEG-TDAIEGEEAENLIRDFVDYVKTNKVVNIDELSS
	HP	${\tt QVGLRTQDTINRIQDLLAEGTITGVIDDRGKFIYITPEELAAVANFIRQRGRVSIAELAQ}$
15		. *****.* . **.******* **.****** *.*.
	CE	${\tt HFGLKSEDAVNRLQHFIEEGLVQGVMDDRGKFIYISDEEFAAVAKFINQRGRVSIHEIAE}$
	HP	ASNSLIAWGRESPAQAPA
		.**.** . *.*.
	CE	QSNRLIRLETPSAAE
20		

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T09311), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10413> (Sequence Number 10, 28, 46)

Determination of the whole base sequence for the cDNA 30 insert of clone HP10413 obtained from the human stomach cancer

45

cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 78 bp, an ORF of 588 bp, and a 3'-nontranslation region of 1209 bp. The ORF codes for a protein consisting of 195 amino acid residues with one transmembrane 5 domain the N-terminal. Figure 11 depicts at hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified 10 upon transduction into the COS7 cells of an expression vector in which a HindIII-PmaCI fragment containing a cDNA fragment encoding the N-terminal 65 amino acid residues in the present protein was inserted at the HindIII-PmaCI site of pSSD3. The in vitro translation resulted in the formation of a translation 15 product of 28 kDa that was somewhat larger than the molecular weight of 21,671 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the swine steroidal membrane-binding protein (GenBank Accession No. X99714). Table 11 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the swine steroidal membrane-binding protein (SS). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 96.4% among the entire regions.

20

46

Table 11

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA021062), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10415> (Sequence Number 11, 29, 47)

Determination of the whole base sequence for the cDNA insert of clone HP10415 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 71 bp, an ORF of 1389 bp, and a 3'-non-translation region of 103 bp. The ORF codes for a protein consisting of 462 amino acid residues with one transmembrane domain at the N-terminal. Figure 12 depicts the hydrophobicity/hydrophilicity profile of the present protein

47

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 48 kDa that was somewhat smaller than the molecular weight of 52,458 predicted from the ORF.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the cytochrome P450 as exemplified by the simian cytochrome P450IIIA8 (SWISS-PROT Accession No. P33268). Table 12 indicates the comparison of the amino acid sequences between 10 the human protein of the present invention (HP) and the simian cytochrome P450IIIA8 (CP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The 15 both proteins possessed a homology of 21.3% among the entire regions.

48

Table 12

	HP	MLDFAIFAVTFLLALVGAVLYLYPASRQAAGIPGITPTEEKDGNLPDIVN-SGSLHEF
		.********
5	CP	${\tt MDLIPDLAVETWLLLAVTLVLLYLYGTHSHGLFKKLGIPGPTPLPLLGNILSYRKGFWTF}$
	HP	LVNLHERYGPVVSFWFGRRLVVSLGTVDVLKQHINPNKTLDPFETMLK-SLLRYQSGGGS
		** * .*. **. * * * *
	CP	DMECYKKYGKVWGFYDGRQPVLAITDPNMIK-TVLVKECYSVFTNRRPFGPVGFMKNAIS
	HP	VSENHMRKKLYENGVTDSLKSNFALLLKLSEELLDKWLSYPET-QHVPLSQHMLGF
10		**. *** * ***
	CP	IAEDEEWKRIRSLLSPTFTSGKLKEMVPIIAKYGDVLVRNLRREAETGKPVTLKDVFGAY
	HP	AMKSVTQMVMGSTF-EDDQEVIRFQKNHGTVWSEIGKGFLDGSLDKNM
		.** .*** *. *. *
	СP	SMDVITSTSFGVNIDSLNNPQDPFVENTKKLLRFDFLDPFFLSITIFPFIIPILEVLNIS
15	HP	TRKKQYEDALMQ-LESVLRNIIKE-RKGR-NFSQHIFIDSLVQGNLNDQQILEDS
		*
	CP	${\tt IFPREVTSFLRKSVKRIKESRLKDTQKHRVDFLQLMIDSQNSKETESHKALSDLELVAQS}$
	HP	${\tt MIFSLASCIITAKLCTWAICFLTTSEEVQKKLYEEINQVF-GNGPVTPEKIEQLRYCQHV}$
		.** .** *. ***. * * * *
20	CP	IIFIFAGYETTSSVLSFIIYELATHPDVQQKLQEEIDTVLPNKAPPTYDTVLQMEYLDMV
	HP	${\tt LCETVRTAKLTPVSAQLQDIEGKIDRFIIPRETLVLYALGVVLQDPNTWPSPHKFDPDRF}$
		. **.*
	HP	${\tt VNETLRIFPIAMRLERVCKKDVEINGIFIPKGVVVMIPSYALHHDPKYWPEPEKFLPERF}$
	HP	DDELVMKTFSSLGFSGTQECPELRFAYMVTTVLLSVLVKRLHLLSVEGQVIETKYE
25		.** ****** * * *
	CP	SKKNNDNIDPYIYTPFG-SGPRNCIGMRFALMNMKLAIIRVLQNFSFKPCKETQIPLKLR
	HP	LVTSSREEAWITVSKRY
		*
	CP	LGGLLQTEKPIVLKIESRDGTVSGA
2 ^		

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs

possessing the homology of 90% or more (for example, Accession No. AA381169), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The cytochrome P450 participates in the drug metabolism and can be utilized as a catalyst in organic synthesis reactions such as oxidation and so on.

<HP10419> (Sequence Number 12, 30, 48)

· 5

Determination of the whole base sequence for the cDNA insert of clone HP10419 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 170 bp, an ORF of 744 bp, and a 3'-non-translation region of 1116 bp. The ORF codes for a protein consisting of 247 amino acid residues with a hydrophobic region of putative seven transmembrane domains. Figure 13 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA340663), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10424> (Sequence Number 13, 31, 49)

Determination of the whole base sequence for the cDNA insert of clone HP10424 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 97 bp, an ORF of 342 bp, and a 3'-non-translation region of 54 bp. The ORF codes for a protein

10

from the ORF.

WO 98/55508 PCT/JP98/02445

50

consisting of 113 amino acid residues with one transmembrane domain at the N-terminal. Figure 14 depicts hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-AccI fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 58 amino acid residues in the present protein was inserted at the HindIII-SmaI site of pSSD3. The in vitro translation resulted in the formation of a translation product of 14 kDa that was somewhat larger than the molecular weight of 12,784 predicted

of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA401979), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10428> (Sequence Number 14, 32, 50)

Determination of the whole base sequence for the cDNA insert of clone HP10428 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 287 bp, an ORF of 1098 bp, and a 3'-non-translation region of 659 bp. The ORF codes for a protein consisting of 365 amino acid residues with a hydrophobic region of putative nine transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile of

the present protein obtained by the Kyte-Doolittle method. The result of the in vitro translation did not reveal the formation of distinct bands and only revealed the formation of smeary

51

bands at the high-molecular-weight position.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the baker's yeast hypothetical membrane protein YML038c (NBRF Accession No. S49741). Table 13 indicates the comparison of the amino acid sequences between the human 10 protein of the present invention (HP) and the baker's yeast hypothetical membrane protein YML038c (SC). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 26.3% among the N-terminal region of 281 amino acid residues.

52

Table 13

	нР	MGRWALDVAFLWKAVLTLGLVL-LYYCFSIGITFYNKWLTKSFHFPLFMTMLHLA
		. *.* *.*
5	sc	MNRTVFLAFVFGWYFCS-IALSIYNRWMFDPKDGLGIGYPVLVTTFHQA
	HP	VIFLFSALSRALVQCSSHRARVVLSWADYLRRVAPTALATALDVGLSNWSFLYVTVS
		****** ** ***** ** ***** ** *****
	sc	TLWLLSGIYIKLRHKPVKNVLRKNNGFNWSFFLKFLLPTAVASAGDIGLSNVSFQYVPLT
	HP	LYTMTKSSAVLFILIFSLIFKLEELRAALVLVVLLIAGGLFMFTYKSTQ-FN
10		.**** *.*. *.*
	sc	IYTIIKSSSIAFVLLFGCIFKLEKFHWKLALSVIIMFVGVALMVFKPSDSTSTKNDQALV
	HP	VEGFALVLGASFIGGIRWTLTQMLLQKAELGLQNPIDTMFHLQPLMFLGLFPLFAVFEGL
		. * *******
	sc	IFGSFLVLASSCLSGLRWVYTQLMLRNNPIQTNTAAAVEES-DGALFTENEDNVDNEPVV
15	HP	HLSTSEKIFRFQDT-GLLLRVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEV
		.* * *. *. ** *******
	sc	NLANNKMLENFGESKPHPIHTIHQLAPIMGITLLLTS-LLVEKPFPGIFS-SSIFRLD
	HP	CTLLLAAHLLGDQISLLNWLGFALCLSGISLHVALKALHSRGDGGPKALKGLGSSPDLEL
20	sc	TSNGGVGTETTVLSIVRGIVLLILPGFAVFLLTICEFSILEQTPVLTVSIVGIVKELLTV
	HP	LLRSSQREEGDNEEEEYFVAQGQQ
	sc	IFGIIILSERLSGFYNWLGMLIIMADVCYYNYFRYKQDLLQKYHSVSTQDNRNELKGFQD
		·

25

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA018345), but it can not be assessed whether these ESTs

with partial sequences code for the same protein as the protein of the present invention.

<HP10429> (Sequence Number 15, 33, 51)

Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 156 bp, an ORF of 681 bp, and a 3'-nontranslation region of 206 bp. The ORF codes for a protein consisting of 226 amino acid residues with four transmembrane domains. Figure 16 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 25 kDa that was almost consistent with the molecular weight of 25,321 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or 20 more (for example, Accession No. AA315933), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10432> (Sequence Number 16, 34, 52)

15

Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human liver cDNA 25 libraries revealed the structure consisting of a 5'-nontranslation region of 28 bp, an ORF of 390 bp, and a 3'-nontranslation region of 554 bp. The ORF codes for a protein consisting of 129 amino acid residues with a signal-like

WO 98/55508

54

PCT/JP98/02445

sequence at the N-terminal and one interior transmembrane domain. Therefore, the present protein is considered to be a type-I membrane protein. Figure 17 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T74424), but the same ORF as that in the present cDNA was not identified.

<HP10433> (Sequence Number 17, 35, 53)

Determination of the whole base sequence for the cDNA insert of clone HP10433 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 72 bp, an ORF of 492 bp, and a 3'-nontranslation region of 131 bp. The ORF codes for a protein consisting of 163 amino acid residues with one transmembrane N-terminal. 20 domain at the Figure 18 depicts hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified 25 upon transduction into the COS7 cells of an expression vector in which a HindIII-Eco81I fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 137 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein

55

is considered to be a type-II membrane protein. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 18,617 predicted from the ORF.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or 10 more (for example, Accession No. H84693), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

<HP10480> (Sequence Number 18, 36, 54)

Determination of the whole base sequence for the cDNA insert of clone HP10480 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 79 bp, an ORF of 582 bp, and a 3'-non-translation region of 1253 bp. The ORF codes for a protein consisting of 193 amino acid residues with four transmembrane domains. Figure 19 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 21,445 predicted from the ORF.

25 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or

56

more (for example, Accession No. W93606), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

The present invention provides human proteins having transmembrane domains and cDNAs encoding said proteins. All of the proteins of the present invention are putative proteins controlling the proliferation and differentiation of the cells, because said proteins exist on the cell membrane. Therefore, the proteins of the present invention can be used as 10 pharmaceuticals or as antigens for preparing antibodies against said proteins. Furthermore, said DNAs can be used for the expression of large amounts of said proteins. The cells expressing large amounts of membrane proteins with transfection of these membrane protein genes can be applied to the detection 15 of the corresponding ligands, the screening of novel low-molecular medicines, and so on.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for

57

analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as 5 molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA 10 sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known in the process of discovering other polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for 15 examination of expression patterns; to raise anti-protein antibodiesusing DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in 20 a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

25 The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in

assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of 15 being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A 20 Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

25 <u>Nutritional Uses</u>

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source

and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation

10 Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

25 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H.

60

Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Po lyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 -Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et

- al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.
- 10 Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols 15 Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); 20 Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined

WO 98/55508

PCT/JP98/02445

62

immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial orfungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein 15 of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, 20 insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or 25 other respiratory problems. Other conditions, in which immune is suppression desired (including, for example, transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be

PCT/JP98/02445 WO 98/55508

63

possible to immune responses, in a number of ways. regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of 5 activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous Tolerance, exposure of the T cells to the suppressive agent. 10 which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent. 15

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in Typically, in tissue transplants, tissue transplantation. rejection of the transplant is initiated through 25 recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2

20

64

activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen blocking antibody), prior B7-1, B7-3) or transplantation can lead to the binding of the molecule to the 5 natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as immunosuppressant. Moreover, the lack of costimulation may 10 also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

25

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor: ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent 10 production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. 15 The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B

66

lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression

67

vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface 10 of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II 15 molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_2 microglobulin protein or an MHC class $II\alpha$ chain protein and an MHC class $II\beta$ chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which 25 blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a

68

T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

5 Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic 10 studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 15 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John

69

Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Thl and CTL responses) include, without limitation, those 5 described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in 10 Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that 15 activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; 20 Nair et al., Journal of 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990. 25

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in:

70

Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in 15 regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation 20 of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the 25 growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently WO 98/55508

71

PCT/JP98/02445

of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation 5 of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal 10 nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo (i.e., or ex-vivo with in conjunction bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney,

M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area cell assay, Ploemacher, R.E. Culture forming In 10 Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., 15 New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

- A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.
- A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the

73

invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, 20 which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a 25 tendon/ligament-like tissue inducing protein prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue

74

formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of 5 tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendonligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of 10 tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as 20 mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized 25 neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders,

WO 98/55508

such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

75

PCT/JP98/02445

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

76

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. W095/16035 (bone, cartilage, tendon); International Patent Publication No. W095/05846 (nerve, neuronal); International Patent Publication No. W091/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

10

A protein of the present invention may also exhibit activinorinhibin-related activities. Inhibins characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of

77

the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

5 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell

78

population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in 15 Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller 20 et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (includinghereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A

protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system 5 vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin.

10 Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res.
45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991);
Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate 15 activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors 20 involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). 25 Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments receptors and ligands) may themselves be useful as inhibitors

of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include

without limitation those described in:Current Protocols in
Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies,
E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and
Wiley-Interscience (Chapter 7.28, Measurement of Cellular
Adhesion under static conditions 7.28.1-7.28.22), Takai et al.,

Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al.,
J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp.
Med. 169:149-160 1989; Stoltenborg et al., J. Immunol.
Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

15 Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by 20 inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can 25 be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis,

81

complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of ytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

20 Other Activities

25

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in

bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, 5 protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent 10 behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related 15 diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another 20 material or entity which is cross-reactive with such protein.

Sequence Table

	(2)	INF	ORMA	TION	FOR	SEQ	ID	NO:	1:							
5		(i) S	EQUE	NCE	CHAR	ACTE	RIST	ics:							
				(A)	LEN	GTH:	382									
				(B)	TYP	E: A	mino	aci	d							
				(D)	TOP	OLOG	Y: L	inea	r							
		(ii)	SEQU	ENCE	KIN	D: P	rote	in							
10		(iii)	HYP	OTHE	TICA	L: N	0								
		(vi)	ORIG	INAL	sou	RCE:									
				(A)	ORG.	ANIS	M: <i>H</i>	ото	sapi	ens					•	
				(B)	CEL	L KI	ND:	Live	r							
15				(D)	CLO	NE N	AME:	HP0	1263							
		(:	xi)	SEQU.	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	1:				
	Met	Gly	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Cys	Ile	Leu	Val	Leu	Cys	Cys
20	1				5					10					15	
	Gly	Ala	Met	Ser	Pro	Pro	Gln	Leu	Ala	Leu	Asn	Pro	Ser	Ala	Leu	Leu
				20					25					30		
	Ser	Arg	Gly	Cys	Asn	Asp	Ser	Asp	Val	Leu	Ala	Val	Ala	Gly	Phe	Ala
			35					40					45			
25	Leu	Arg	Asp	Ile	Asn	Lys	Asp	Arg	Lys	Asp	Gly	Tyr	Val	Leu	Arg	Leu
		50					55					60				
	Asn	Arg	Val	Asn	Asp	Ala	Gln	Glu	Tyr	Arg	Arg	Gly	Gly	Leu	Gly	Ser
	65					70	•				75	•				80
	Leu	Phe	Tyr	Leu	Thr	Leu	Asp	Val	Leu	Glu	Thr	Asp	Cys	His	Val	Leu
30					85					90					95	
	Arg	Lys	Lys	Ala	Trp	Gln	Asp	Cys	Gly	Met	Arg	Ile	Phe	Phe	Glu	Ser
	*			100					105					110		
	Val	Tyr	Gly	Gln	Cys	Lys	Ala	Ile	Phe	Tyr	Met	Asn	Asn	Pro	Ser	Arg
			115					120					125			
35	Val	Leu	Tyr	Leu	Ala	Ala	Tyr	Asn	Cys	Thr	Leu	Arg	Pro	Val	Ser	Lys
		130					135					140				
	Lys	Lys	Ile	Tyr	Met	Thr	Cys	Pro	Asp	Cys	Pro	Ser	Ser	Ile	Pro	Thr

	Asp	Ser	Ser	Asn	His	Gln	Val	Leu	Glu	Ala	Ala	Thr	Glu	Ser	Leu	Ala
					165					170					175	
	Lys	Tyr	Asn	Asn	Glu	Asn	Thr	Ser	Lys	Gln	Tyr	Ser	Leu	Phe	Lys	Val
				180					185					190		
5	Thr	Arg	Ala	Ser	Ser	Gln	Trp	Val	Val	Gly	Pro	Ser	Tyr	Phe	Val	Glu
			195					200					205			
	Tyr	Leu	Ile	Lys	Glu	Ser	Pro	Cys	Thr	Lys	Ser	Gln	Ala	Ser	Ser	Cys
		210					215					220				
	Ser	Leu	Gln	Ser	Ser	Asp	Ser	Val	Pro	Val	G1y	Leu	Cys	Lys	Gly	Ser
10	225					230					235		-	-		240
	Leu	Thr	Arg	Thr	His	Trp	Glu	Lys	Phe	Val	Ser	Val	Thr	Cys	Asp	Phe
					245			•		250					255	
	Phe	Glu	Ser	Gln	Ala	Pro	Ala	Thr	Gly	Ser	Glu	Asn	Şer	Ala	Val	Asn
				260					265					270		
15	Gln	Lys	Pro	Thr	Asn	Leu	Pro	Lys	Val	Glu	Glu	Ser	Gln	Gln	Lys	Asn
			275					280					285		,	
	Thr	Pro	Pro	Thr	Asp	Ser	Pro	Ser	Lvs	Ala	Glv	Pro		Gly	Ser	Va1
		290			•		295		_, _		,	300		,		
	Gln	Tyr	Leu	Pro	Asp	Leu		Asp	Lvs	Asn	Ser		Glu	Lys	G1v	Pro
20	305	,				310			-,-		315			_, -	,	320
		Glu	Ala	Phe	Pro		His	Len	Aen	Ĭ.e.n		Thr	Aen	Pro	G1n	
					325	,		504	р	330	1111	1111	11511	110	335	01)
	G111	Thr	Len	Aen		Sar	Pho	Lau	Dha		C1.,	Dro	Ma+	Glu		Ive
	024	••••	Deu	340	110	361	THE	Deu	345	nen	GIU	110	riec	350	GIU	Бyз
25	ĭ eu	V = 1	Va 1		Dro	Pho	Dro	T 0		Io	41 =	A == ==	ጥե	Ala	C1	C** 0
23	Leu	AUT	355	rea	FIO	FILE	PLO	360	GLU	rys	AIA	Arg		AIR	Glu	cys
	Dro	CI.		۸1.	C1-	40-	A 7		D	*	17 - 1	•	365	D		
	. FLO		PEO	Ala	GII	ASI		ser	PIO	Leu	vaı		rro	rro		
		370					375					380				
30																

- (2) INFORMATION FOR SEQ ID NO: 2:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 317
 - (B) TYPE: Amino acid
- 35 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No

WO 98/55508

PCT/JP98/02445

85

(vi) ORIGINAL SOURC

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Liver

(D) CLONE NAME: HP01299

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

	Met	Trp	Leu	Tyr	Leu	Ala	Ala	Phe	Val	Gly	Leu	Tyr	Tyr	Leu	Leu	His
	1				5					10					15	
10	Trp	Tyr	Arg	Glu	Arg	Gln	Val	Va1	Ser	His	Leu	Gln	Asp	Lys	Tyr	Val
				20					25					30		
	Phe	Ile	Thr	Gly	Cys	Asp	Ser	Gly	Phe	Gly	Asn	Leu	Leu	Ala	Arg	Gln
			35					40					45			
	Leu	Asp	Ala	Arg	Gly	Leu	Arg	Val	Leu	Ala	Ala	Cys	Leu	Thr	Glu	Lys
L5		50					55					60				
	Gly	Ala	Glu	Gln	Leu	Arg	Gly	Gln	Thr	Ser	Asp	Arg	Leu	Glu	Thr	Val
	65					70					75					80
	Thr	Leu	Asp	Val	Thr	Lys	Met	Glu	Ser	Ile	Ala	Ala	Ala	Thr	Gln	Trp
					85					90					95	
20	Val	Lys	Glu	His	Val	Gly	Asp	Arg	Gly	Leu	Trp	Gly	Leu	Val	Asn	Asn
				100					105					110		
	Ala	Gly	Ile	Leu	Thr	Pro	Ile	Thr	Leu	Cys	Glu	Trp	Leu	Asn	Thr	Glu
			115					120					125			
	Asp	Ser	Met	Asn	Met	Leu	Lys	Val	Asn	Leu	Ile	Gly	Val	Ile	Gln	Val
25		130		•			135					140				
	Thr	Leu	Ser	Met	Leu	Pro	Leu	Val	Arg	Arg	Ala	Arg	Gly	Arg	Ile	Val
	145					150					155					160
	Asn	Val	Ser	Ser	Ile	Leu	Gly	Arg	Val	Ala	Phe	Phe	Val	Gly	Gly	Tyr
					165					170					175	
30	Cys	Val	Ser	Lys	Tyr	Gly	Val	Glu	Ala	Phe	Ser	Asp	Ile	Leu	Arg	Arg
				180					185					190		
	Glu	Ile	Gln	His	Phe	Gly	Val	Lys	Ile	Ser	Ile	Val	Glu	Pro	Gly	Tyr
			195					200					205			
	Phe	Arg	Thr	Gly	Met	Thr	Asn	Met	Thr	Gln	Ser	Leu	Glu	Arg	Met	Lys
35		210					215					220				
	Gln	Ser	Trp	Lys	Glu	Ala	Pro	Lys	His	Ile	Lys	Glu	Thr	Tyr	Gĺy	Gln
	225					230					235					240
	Gln	Tyr	Phe	Asp	Ala	Leu	Tyr	Asn	Ile	Met	Lys	Glu	Gly	Leu	Leu	Asn

PCT/JP98/02445

WO 98/55508 86 245 250 255 Cys Ser Thr Asn Leu Asn Leu Val Thr Asp Cys Met Glu His Ala Leu 260 265 270 Thr Ser Val His Pro Arg Thr Arg Tyr Ser Ala Gly Trp Asp Ala Lys 5 280 Phe Phe Phe Ile Pro Leu Ser Tyr Leu Pro Thr Ser Leu Ala Asp Tyr 290 295 300 Ile Leu Thr Arg Ser Trp Pro Lys Pro Ala Gln Ala Val 305 310 315 10 (2) INFORMATION FOR SEQ ID NO: 3: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 296 15 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Liver (D) CLONE NAME: HP01347 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

25

Met Ser Asp Ser Lys Glu Pro Arg Val Gln Gln Leu Gly Leu Leu Gly 10 Cys Leu Gly His Gly Ala Leu Val Leu Gln Leu Leu Ser Phe Met Leu 30 20 25 30 Leu Ala Gly Val Leu Val Ala Ile Leu Val Gln Val Ser Lys Val Pro 40 Ser Ser Leu Ser Gln Glu Gln Ser Glu Gln Asp Ala Ile Tyr Gln Asn 50 55 35 Leu Thr Gln Leu Lys Ala Ala Val Gly Glu Leu Ser Glu Lys Ser Lys 65 70 Leu Gln Glu Ile Tyr Gln Glu Leu Thr Gln Leu Lys Ala Ala Val Gly 90 95

	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr
				100					105					110		
	Arg	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln
			115					120					125			
5	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	Arg	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu
		130					135					140				
	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	Arg	Leu
	145					150					155					160
	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile
10					165					170					175	
	Tyr	Gln	Glu	Leu	Thr	Glu	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu
				180					185					190		
	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	G1n	Leu	Lys	Ala
			195					200					205			
15	Ala	Val	Gly	Glu	Leu	Pro	Asp	Gln	Ser	Lys	G1n	Gln	Gln	Ile	Tyr	Gln
		210					215					220				
	Glu	Leu	Thr	Asp	Leu	Lys	Thr	Ala	Phe	Glu	Arg	Leu	Cys	Arg	His	Cys
	225					230				٠	235					240
	Pro	Lys	Asp	Trp	Thr	Phe	Phe	Gln	Gly	Asn	Cys	Tyr	Phe	Met	Ser	Asn
20					245					250					255	
	Ser	Gln	Arg	Asn	Trp	His	Asp	Ser	Val	Thr	Ala	Cys	Gln	Glu	Val	Arg
				260					265					270		
	Ala	Gln		Va1	Va1	Ile	Lys	Thr	Ala	Glu	Glu	Gln	Leu	Pro	Ala	Val
•			275					280					285			
25	Leu		Gln	Trp	Arg	Thr	Gln	Gln								
		290	•				295									

- (2) INFORMATION FOR SEQ ID NO: 4:
- 30 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 197
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
- 35 (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens

88

(B)	CELL	KIND:	Stomach	cancer
-----	------	-------	---------	--------

(D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

5 Met Cys Thr Gly Lys Cys Ala Arg Cys Val Gly Leu Ser Leu Ile Thr 5 Leu Cys Leu Val Cys Ile Val Ala Asn Ala Leu Leu Leu Val Pro Asn 25 10 Gly Glu Thr Ser Trp Thr Asn Thr Asn His Leu Ser Leu Gln Val Trp 35 40 45 Leu Met Gly Gly Phe Ile Gly Gly Gly Leu Met Val Leu Cys Pro Gly Ile Ala Ala Val Arg Ala Gly Gly Lys Gly Cys Cys Gly Ala Gly Cys 15 70 75 Cys Gly Asn Arg Cys Arg Met Leu Arg Ser Val Phe Ser Ser Ala Phe 90 Gly Val Leu Gly Ala Ile Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu 105 20 Arg Asn Gly Pro Arg Cys Leu Met Asn Gly Glu Trp Gly Tyr His Phe 115 125 Glu Asp Thr Ala Gly Ala Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg 135 140 Cys Glu Ala Pro Pro Arg Val Val Pro Trp Asn Val Thr Leu Phe Ser 25 145 150 155 160 Leu Leu Val Ala Ala Ser Cys Leu Glu Ile Val Leu Cys Gly Ile Gln 170 Leu Val Asn Ala Thr Ile Gly Val Phe Cys Gly Asp Cys Arg Lys Lys 180 185 190 30 Gln Asp Thr Pro His

- (2) INFORMATION FOR SEQ ID NO: 5:
 - (i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 221

- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: Protein

5

89

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP01526

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

10	Met	Glu	Ala	Gly	Gly	Phe	Leu	Asp	Ser	Leu	Ile	Tyr	Gly	Ala	Cys	Val
	1			-	5					10		•			15	
	Val	Phe	Thr	Leu	Gly	Met	Phe	Ser	Ala	Gly	Leu	Ser	Asp	Leu	Arg	His
				20					25					30		
	Met	Arg	Met	Thr	Arg	Ser	Val	Asp	Asn	Val	Gln	Phe	Leu	Pro	Phe	Leu
15			35					40					45			
	Thr	Thr	Glu	Val	Asn	Asn	Leu	Gly	Trp	Leu	Ser	Tyr	Gly	Ala	Leu	Lys
		50					55					60				
	Gly	Asp	Gly	Ile	Leu	Ile	Val	Val	Asn	Thr	Val	Gly	Ala	Ala	Leu	Gln
	65					70					75					80
20	Thr	Leu	Tyr	Ile	Leu	Ala	Tyr	Leu	His	Tyr	Cys	Pro	Arg	Lys	Arg	Val
					85		•			90					95	
	Val	Leu	Leu	Gln	Thr	Ala	Thr	Leu	Leu	Gly	Val	Leu	Leu	Leu	Gly	Tyr
				100					105					110		
0_	Gly	Tyr		Trp	Leu	Leu	Val		Asn	Pro	Glu	Ála	_	Leu	Gln	Gln
25			115					120					125			
	Leu		Leu	Phe	Cys	Ser		Phe	Thr	Ile	Ser		Tyr	Leu	Ser	Pro
		130		_		_	135				_	140			_	_
		Ala	Asp	Leu	Ala	Lys	Val	Ile	Gln	Thr	-	Ser	Thr	Gln	Cys	
30	145	M	D	¥	m1	150		m 1			155	•		.		160
30	ser	ıyr	Pro	Leu	165	Ile	AIA	Thr	Leu		Thr	ser	AIA	ser		cys
	Lou	T	C1	Dho		1	A == =	4	7	170	T1.	Wa n	W- 1	C	175	Dho
	Leu	1 7 1	GIY	180	urg	Leu	ALG	Asp	185	lyr	IIe	met	vai	190	ASII	File
	Pro	G1 v	٦١م		Thr	Ser	Pho	T1 A		Dho	ሞተካ	1 011	Dha		Lve	ጥህታ
35		019	195	141	1111	561	Inc	200	AL S	THE	пр	beu	205	ırþ	шуз	1 9 2
	Pro	Gln		G1n	Asp	Arg	Asn		Trn	Ĭ.eu	I.e.u	GIr				
		210			P	5	215	- / -	P	Dou	Lu	220				

WO 98/55508

90

PCT/JP98/02445

(2)	INFURI	TATION	FUK	2 F.Q	ΤD	NO:	0:	
	(i)	SEQUE	NCE (CHARA	CTI	ERIST	rics	3:

- (A) LENGTH: 251
- (B) TYPE: Amino acid
- 5 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10230

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

15 Met Ser Asp Ile Gly Asp Trp Phe Arg Ser Ile Pro Ala Ile Thr Arg Tyr Trp Phe Ala Ala Thr Val Ala Val Pro Leu Val Gly Lys Leu Gly 25 20 Leu Ile Ser Pro Ala Tyr Leu Phe Leu Trp Pro Glu Ala Phe Leu Tyr 35 40 Arg Phe Gln Ile Trp Arg Pro Ile Thr Ala Thr Phe Tyr Phe Pro Val 55 60 Gly Pro Gly Thr Gly Phe Leu Tyr Leu Val Asn Leu Tyr Phe Leu Tyr 25 65 70 Gin Tyr Ser Thr Arg Leu Glu Thr Gly Ala Phe Asp Gly Arg Pro Ala Asp Tyr Leu Phe Met Leu Leu Phe Asn Trp Ile Cys Ile Val Ile Thr 100 105 110 30 Gly Leu Ala Met Asp Met Gln Leu Leu Met Ile Pro Leu Ile Met Ser 120 Val Leu Tyr Val Trp Ala Gln Leu Asn Arg Asp Met Ile Val Ser Phe 135 140 Trp Phe Gly Thr Arg Phe Lys Ala Cys Tyr Leu Pro Trp Val Ile Leu 35 145 150 155 Gly Phe Asn Tyr Ile Ile Gly Gly Ser Val Ile Asn Glu Leu Ile Gly 170

Asn Leu Val Gly His Leu Tyr Phe Phe Leu Met Phe Arg Tyr Pro Met

WO 98/55508

				180					185					190	•	
	Asp	Leu	Gly	Gly	Arg	Asn	Phe	Leu	Ser	Thr	Pro	Gln	Phe	Leu	Tyr	Arg
			195					200					205			
	Trp	Leu	Pro	Ser	Arg	Arg	Gly	Gly	Val	Ser	Gly	Phe	Gly	Val	Pro	Pro
5		210					215					220				
	Ala	Ser	Met	Arg	Arg	Ala	Ala	Asp	Gln	Asn	Gly	Gly	Gly	Gly	Arg	His
	225					230					235					240
	Asn	Trp	Gly	Gln	Gly	Phe	Arg	Leu	Gly	Asp	Gln					
					245					250						
10						٠										
	(2)	INF	ORMA!	rion	FOR	SEQ	ID	NO:	7:							
		(i) S	EQUEI	NCE (CHAR	ACTE	RIST	ics:							
				(A)	LEN	GTH:	106									
15				(B)	TYP	E: A	nino	aci	d							
				(D)	TOP	OLOG	Y: L	inea	r							
		(.	ii) S	SEQUI	ence	KIN	D: P:	rote	in							
		(:	iii)	HYPO	THE:	rica	L: N	0								
20		(vi) (ORIG:	INAL	SOUT	RCE:									
				(A)	ORGA	ANIS	1: H	omo .	sapi	ens						
				(B)	CELI	L KI	ND:	Epide	ermo	id ca	arci	noma				
				(C)	CELI	LII	NE: 1	KB								
				(D)	CLO	NE NA	AME:	HP1	389							
25																
		(;	xi) S	EQUE	ENCE	DESC	CRIP'	rion	: SEC) ID	NO:	7:				
		Ala	Thr	Pro		Pro	Val	Ile	Pro		Val	Pro	Phe	Glu		Ser
	1				5					10					15	
30	Lys	Pro	Pro		Ile	Glu	Gly	Leu		Pro	Thr	Val	Tyr		Asn	Pro
				20					25					30		
	Glu	Ser	Phe	Lys	Glu	Lys	Phe		Arg	Lys	Thr	Arg	Glu	Asn	Pro	Val
			35					40					45			
	Val		Ile	Gly	Cys	Leu	Ala	Thr	Ala	Ala	Ala	Leu	Thr	Tyr	Gly	Leu
35	_	50					55					60				
		Ser	Phe	His	Arg		Asn	Ser	Gln	Arg		Gln	Leu	Met	Met	
	65	_			_	70					75					80
	Thr	Arg	Ile	Ala	Ala	Gln	Gly	Phe	Thr	Val	Ala	Ala	Ile	Leu	Leu	Gly

92

85 90 95

Leu Ala Val Thr Ala Met Lys Ser Arg Pro 100 105

5

- (2) INFORMATION FOR SEQ ID NO: 8:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 78
- 10 (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - 15 (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10408
 - 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr Leu Leu Gly Ser

1 5 10 15

Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu Lys Leu Lys Glu

25 20 25 30

Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe Leu Glu Leu Leu

5 40 45

Glu Lys Leu Cys Leu Leu His Leu Pro Ser Gly Thr Ser Val Thr

50 55 60

30 Leu His His Ala Arg Ser Gln His His Val Val Cys Asn Thr

65 70 75

- (2) INFORMATION FOR SEQ ID NO: 9:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 314
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear

93

(ii)	SEQUENCE	KIND:	Protein
(iii)	HYPOTHE	TICAL:	No

(vi) ORIGINAL SOURCE:

210

5 (A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10412

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9: 10 Met Val Ala Pro Val Trp Tyr Leu Val Ala Ala Ala Leu Leu Val Gly Phe Ile Leu Phe Leu Thr Arg Ser Arg Gly Arg Ala Ala Ser Ala Gly 25 15 Gln Glu Pro Leu His Asn Glu Glu Leu Ala Gly Ala Gly Arg Val Ala 40 Gln Pro Gly Pro Leu Glu Pro Glu Glu Pro Arg Ala Gly Gly Arg Pro 55 Arg Arg Arg Arg Asp Leu Gly Ser Arg Leu Gln Ala Gln Arg Arg Ala 20 70 75 Gin Arg Val Ala Trp Ala Glu Ala Asp Glu Asn Glu Glu Glu Ala Val Ile Leu Ala Gln Glu Glu Glu Gly Val Glu Lys Pro Ala Glu Thr His 105 25 Leu Ser Gly Lys Ile Gly Ala Lys Lys Leu Arg Lys Leu Glu Glu Lys 115 120 125 Gin Ala Arg Lys Ala Gin Arg Glu Ala Glu Glu Ala Glu Arg Glu Glu 135 Arg Lys Arg Leu Glu Ser Gln Arg Glu Ala Glu Trp Lys Lys Glu Glu 30 145 150 Glu Arg Leu Arg Leu Glu Glu Glu Glu Glu Glu Glu Glu Arg Lys 170 Ala Arg Glu Glu Gln Ala Gln Arg Glu His Glu Glu Tyr Leu Lys Leu 180 185 35 Lys Glu Ala Phe Val Val Glu Glu Glu Gly Val Gly Glu Thr Met Thr 200 205 Glu Glu Gln Ser Gln Ser Phe Leu Thr Glu Phe Ile Asn Tyr Ile Lys

215

94

Gln Ser Lys Val Val Leu Leu Glu Asp Leu Ala Ser Gln Val Gly Leu 225 230 235 240 Arg Thr Gln Asp Thr Ile Asn Arg Ile Gln Asp Leu Leu Ala Glu Gly 245 250 Thr Ile Thr Gly Val Ile Asp Asp Arg Gly Lys Phe Ile Tyr Ile Thr 265 Pro Glu Glu Leu Ala Ala Val Ala Asn Phe Ile Arg Gln Arg Gly Arg 275 280 285 Val Ser Ile Ala Glu Leu Ala Gln Ala Ser Asn Ser Leu Ile Ala Trp 10 295 300 Gly Arg Glu Ser Pro Ala Gln Ala Pro Ala 305 310 15 (2) INFORMATION FOR SEQ ID NO: 10: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 195 (B) TYPE: Amino acid (D) TOPOLOGY: Linear 20 (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens 25 (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10413 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10: 30 Met Ala Ala Glu Asp Val Val Ala Thr Gly Ala Asp Pro Ser Asp Leu Glu Ser Gly Gly Leu Leu His Glu Ile Phe Thr Ser Pro Leu Asn Leu 25 20 Leu Leu Cly Leu Cys Ile Phe Leu Leu Tyr Lys Ile Val Arg Gly 35 40 Asp Gln Pro Ala Ala Ser Gly Asp Ser Asp Asp Asp Glu Pro Pro

55

Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro Ala Glu Leu Arg Arg

VO 98/55508	70 cm (YP)00 (03 4 4 5
VU 98/2221X	PCT/JP98/02445

	65					70					75					80
		Asp	Glv	Val	Gln		Pro	Arg	Ile	Leu		Ala	Ile	Asn	G1v	Lvs
		•			85	•		0		90					95	•
	Va1	Phe	Asp	Va1		Lvs	G1v	Arg	Lvs		Tvr	Glv	Pro	Glu	G1v	Pro
5				100		, -	,	******	105	- 110	-,-	,		110	,	
•	Tvr	Glv	Val		Ala	Glv	Arg	Asp		Ser	Arg	Glv	Leu	Ala	Thr	Phe
	,	,	115					120				,	125			
	Cvs	Leu		Lvs	Glu	Ala	Leu		Asp	Glu	Tvr	Asp		Leu	Ser	Asp
	-,-	130		, -			135	-,-			-,-	140	P			
10	Leu		Ala	Ala	G1n	Gln		Thr	Leu	Ser	Asp		Glu	Ser	Gln	Phe
	145					150					155					160
		Phe	Lvs	Tvr	His		Val	Glv	Lvs	Leu		Lvs	Glu	Gly	G1u	
					165		_	,	_, _	170		-,-		,	175	
	Pro	Thr	Val	Tyr		Asp	Glu	Glu	Glu		Lvs	Asp	Glu	Ser		Arg
15				180					185		-,-			190		
	Lys	Asn	Asp													
			195													
20	(2)	INFO	ORMA?	rion	FOR	SEQ	ID N	NO: 1	11:							
				EQUE												
				-	LENG											
				(B)	TYPE	E: An	nino	acid	i							
				(D)	TOPO	LOGY	: Li	inear	:							
25		(:	ii) S	EQUE	ENCE	KINI): Pr	otei	in							
		(:	lii)	HYPO	THE	CICAI	_: No)								
		(1	/i) (ORIG	INAL	SOUT	RCE:									
				(A)	ORGA	NISN	1: H	omo s	sapie	ens						
30				(B)	CELI	. KIN	ND: 5	Stoma	ch c	ance	er					
				(D)	CLO	IE NA	ME:	HP10	0415							
		()	ci) S	EQUE	ENCE	DESC	RIPI	:NOI	SEC] ID	NO:	11:				
35	Met	Leu	Asp	Phe	Ala	Ile	Phe	Ala	Val	Thr	Phe	Leu	Leu	Ala	Leu	Val
	1				5					10					15	
	Gly	Ala	Val	Leu	Tyr	Leu	Tyr	Pro	Ala	Ser	Arg	Gln	Ala	Ala	Gly	Ile
				20					25					30		

	Pro	Gly	Ile	Thr	Pro	Thr	Glu	Glu	Lys	Asp	Gly	Asn	Leu	Pro	Asp	Ile
			35					40					45			
	Val	Asn	Ser	Gly	Ser	Leu	His	Glu	Phe	Leu	Val	Asn	Leu	His	Glu	Arg
		50					55					60				
5	Tyr	Gly	Pro	Val	Val	Ser	Phe	Trp	Phe	Gly	Arg	Arg	Leu	Val	Val	Ser
	65					70					75					80
	Leu	Gly	Thr	Val	Asp	Val	Leu	Lys	Gln	His	Ile	Asn	Pro	Asn	Lys	Thr
					85					90					95	
	Leu	Asp	Pro	Phe	Glu	Thr	Met	Leu	Lys	Ser	Leu	Leu	Arg	Tyr	Gln	Ser
10				100					105					110		
	Gly	Gly	Gly	Ser	Val	Ser	Glu	Asn	His	Met	Arg	Lys	Lys	Leu	Tyr	Glu
			115					120					125			
	Asn	Gly	Val	Thr	Asp	Ser	Leu	Lys	Ser	Asn	Phe	Ala	Leu	Leu	Leu	Lys
		130					135					140				•
15	Leu	Ser	Glu	Glu	Leu	Leu	Asp	Lys	Trp	Leu	Ser	Tyr	Pro	Glu	Thr	Gln
	145					150					155					160
	His	Val	Pro	Leu	Ser	Gln	His	Met	Leu	Gly	Phe	Ala	Met	Lys	Ser	Val
					165					170					175	
	Thr	Gln	Met	Val	Met	Gly	Ser	Thr	Phe	Glu	Asp	Asp	Gln	Glu	Val	Ile
20				180					185					190		
	Arg	Phe	Gln	Lys	Asn	His	Gly	Thr	Val	Trp	Ser	Glu	Ile	Gly	Lys	Gly
			195					200					205			
	Phe	Leu	Asp	Gly	Ser	Leu	Asp	Lys	Asn	Met	Thr	Arg	Lys	Lys	Gln	Tyr
		210					215					220				
25	Glu	Asp	Ala	Leu	Met	Gln	Leu	Glu	Ser	Val	Leu	Arg	Asn	Ile	Ile	Lys
	225					230					235					240
	Glu	Arg	Lys	Gly	Arg	Asn	Phe	Ser	Gln	His	Ile	Phe	Ile	Asp	Ser	Leu
					245					250					255	
	Val	Gln	Gly	Asn	Leu	Asn	Asp	Gln	Gln	Ile	Leu	Glu	Asp	Ser	Met	Ile
30				260					265					270		
	Phe	Ser	Leu	Ala	Ser	Cys	Ile	Ile	Thr	Ala	Lys	Leu	Cys	Thr	Trp	Ala
			275					280					285			
	Ile	Cys	Phe	Leu	Thr	Thr	Ser	Glu	Glu	Val	Gln	Lys	Lys	Leu	Tyr	Glu
		290					295					300				
35	Glu	Ile	Asn	Gln	Val	Phe	Gly	Asn	Gly	Pro	Val	Thr	Pro	Glu	Lys	Ile
	305				-	310			-		315		-			320
	Glu	Gln	Leu	Arg	Tyr	Cys	Gln	His	Va1	Leu	Cys	Glu	Thr	Val	Arg	Thr
					325					330					335	

	Ala	Lys	Leu	Thr	Pro	Val	Ser	Ala	Gln	Leu	Gln	Asp	Ile		Gly	Ly
				340					345					350		
	Ile	Asp	Arg	Phe	Ile	Ile	Pro	Arg	Glu	Thr	Leu	Val	Leu	Tyr	Ala	Le
			355					360					365			
5	Gly	Val	Val	Leu	Gln	Asp	Pro	Asn	Thr	Trp	Pro	Ser	Pro	His	Lys	Phe
		370					375					380				
	Asp	Pro	Asp	Arg	Phe	Asp	Asp	Glu	Leu	Val	Met	Lys	Thr	Phe	Ser	Se
	385					390					395					400
	Leu	Gly	Phe	Ser	Gly	Thr	Gln	Glu	Cys	Pro	G1u	Leu	Arg	Phe	Ala	Ту
LO					405	,				410					415	
	Met	Val	Thr	Thr	Val	Leu	Leu	Ser	Val	Leu	Val	Lys	Arg	Leu	His	Let
				420					425					430		
	Leu	Ser	Val	Glu	Gly	Gln	Val	Ile	Glu	Thr	Lys	Tyr	Glu	Leu	Val	Thi
			435					440					445			
L 5	Ser	Ser	Arg	Glu	Glu	Ala	Trp	Ile	Thr	Val	Ser	Lys	Arg	Tyr		
		450					455					460				
	(2)	INFO	ORMA'	rion	FOR	SEQ	ID N	10: 1	12:							
20		(i	i) SI	EQUE	NCE (CHARA	CTE	RIST	cs:							
				(A)	LENC	STH:	247									
				(B)	TYPI	E: An	nino	acio	i							
				(D)	TOPO	DLOGY	: Li	inear	•							
		(3	ii) S	SEQUE	ENCE	KINI): Pr	otei	ln							
25		(<u>1</u>	lii)	HYPO	THE	TICAI	.: No)								
		(1	7i) (ORIG	INAL	sour	CE:	•								
				(A)	ORGA	NISN	1: H	omo s	sapie	ens						
				(B)	CELI	L KIN	ID: S	Stoma	ich d	ance	er					
30				(D)	CLO	NE NA	ME:	HP10)419							
		(3	(i) S	SEQUI	ENCE	DESC	RIP	NOI?	SEC] ID	NO:	12:				
				•						•		•				
	Met	Gly	Ala	Ala	Val	Phe	Phe	Gly	Cys	Thr	Phe	Val	Ala	Phe	G1y	Pro
35	1				5			•	-	10					15	
	Ala	Phe	Ala	Leu	Phe	Leu	Ile	Thr	Val	Ala	Gly	Asp	Pro	Leu	Arg	Val
		•		20					25		٠	-		30	-	
	Ile	Ile	Leu	Val	Ala	Glv	Ala	Phe	Phe	Trn	Leu	Val	Ser	Leu	Leu	Leu

			35					40					45			
	Ala	Ser	Val	Val	Trp	Phe	Ile	Leu	Val	His	Val	Thr	Asp	Arg	Ser	Asp
		50					55					60				
	Ala	Arg	Leu	Gln	Tyr	Gly	Leu	Leu	Ile	Phe	Gly	Ala	Ala	Val	Ser	Val
5	65					70					75					80
	Leu	Leu	Gln	Glu	Val	Phe	Arg	Phe	Ala	Tyr	Tyr	Lys	Leu	Leu	Lys	Lys
					85					90					95	
	Ala	Asp	Glu	Gly	Leu	Ala	Ser	Leu	Ser	Glu	Asp	Gly	Arg	Ser	Pro	Ile
				100	•				105				•	110		
10	Ser	Ile	Arg	Gln	Met	Ala	Tyr	Val	Ser	Gly	Leu	Ser	Phe	Gly	Ile	Ile
			115					120					125			
	Ser	Gly	Val	Phe	Ser	Val	Ile	Asn	Ile	Leu	Ala	Asp	Ala	Leu	Gly	Pro
		130					135					140				
	Gly	Val	Val	Gly	Ile	His	Gly	Asp	Ser	Pro	Tyr	Tyr	Phe	Leu	Thr	Ser
15	145					150					155	•				160
	Ala	Phe	Leu	Thr	Ala	Ala	Ile	Ile	Leu	Leu	His	Thr	Phe	Trp	Gly	Val
					165					170					175	
	Val	Phe	Phe		Ala	Cys	Glu	Arg	Arg	Arg	Tyr	Trp	Ala	Leu	Gly	Leu
••				180					185					190		
20	Val	Val		Ser	His	Leu	Leu		Ser	Gly	Leu	Thr		Leu	Asn	Pro
	_	<u>.</u>	195					200					205			
			Glu	Ala	Ser	Leu	Leu	Pro	Ile	Tyr	Ala		Thr	Val	Ser	Met
		210	_				215					220				
2.5		Leu	Trp	Ala	Phe		Thr	Ala	Gly	Gly		Leu	Arg	Ser	Ile	
25	225	_		_		230					235					240
	Arg	Ser	Leu	Leu	-	Lys	Asp									
					245											

- 30 (2) INFORMATION FOR SEQ ID NO: 13:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 35 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:

PCT/JP98/02445 WO 98/55508

99

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10424

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Met Asn Phe Tyr Leu Leu Leu Ala Ser Ser Ile Leu Cys Ala Leu Ile 1

5 15 10

Val Phe Trp Lys Tyr Arg Arg Phe Gln Arg Asn Thr Gly Glu Met Ser

10 25

Ser Asn Ser Thr Ala Leu Ala Leu Val Arg Pro Ser Ser Ser Gly Leu 35

40 45 Ile Asn Ser Asn Thr Asp Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg

55

15 Asp Ile Leu Asn Asn Phe Pro His Ser Ile Ala Arg Gln Lys Arg Ile 70 75

Leu Val Asn Leu Ser Met Val Glu Asn Lys Leu Val Glu Leu Glu His

85 90

Thr Leu Leu Ser Lys Gly Phe Arg Gly Ala Ser Pro His Arg Lys Ser 20 110 105

Thr

(2) INFORMATION FOR SEQ ID NO: 14:

25 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 365
- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: Protein
- 30 (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Epidermoid carcinoma

35 (C) CELL LINE: KB

- (D) CLONE NAME: HP10428
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

	Met	Gly	Arg	Trp	Ala	Leu	Asp	Val	Ala	Phe	Leu	Trp	Lys	Ala	Val	Leu
	1				5					10					15	
	Thr	Leu	Gly	Leu	Val	Leu	Leu	Tyr	Tyr	Cys	Phe	Ser	Ile	Gly	Ile	Thr
				20					25					30		
5	Phe	Tyr	Asn	Lys	Trp	Leu	Thr	Lys	Ser	Phe	His	Phe	Pro	Leu	Phe	Met
			35					40					45			
	Thr	Met	Leu	His	Leu	Ala	Val	Ile	Phe	Leu	Phe	Ser	Ala	Leu	Ser	Arg
		50					55					60				
	Ala	Leu	Val	Gln	Cys	Ser	Ser	His	Arg	Ala	Arg	Val	Val	Leu	Ser	Trp
10	65					70					75					80
	Ala	Asp	Tyr	Leu	Arg	Arg	Val	Ala	Pro	Thr	Ala	Leu	Ala	Thr	Ala	Leu
					85					90					95	
	Asp	Val	Gly	Leu	Ser	Asn	Trp	Ser	Phe	Leu	Tyr	Val	Thr	Val	Ser	Leu
				100					105					110		
15	Tyr	Thr	Met	Thr	Lys	Ser	Ser	Ala	Val	Leu	Phe	Ile	Leu	Ile	Phe	Ser
			115					120					125			
	Leu	Ile	Phe	Lys	Leu	Glu	Glu	Leu	Arg	Ala	Ala	Leu	Val	Leu	Val	Val
		130					135					140	,			
	Leu	Leu	Ile	Ala	Gly	Gly	Leu	Phe	Met	Phe	Thr	Tyr	Lys	Ser	Thr	Gln
20	145					150					155					160
	Phe	Asn	Val	Glu	Gly	Phe	Ala	Leu	Val	Leu	Gly	Ala	Ser	Phe	Ile	Gly
					165					170					175	
	Gly	Ile	Arg	Trp	Thr	Leu	Thr	Gln	Met	Leu	Leu	Gln	Lys	Ala	Glu	Leu
				180					185					190		
25	Gly	Leu	Gln	Asn	Pro	Ile	Asp	Thr	Met	Phe	His	Leu	Gln	Pro	Leu	Met
			195					200					205			
	Phe	Leu	G1y	Leu	Phe	Pro	Leu	Phe	Ala	Val	Phe	Glu	Gly	Leu	His	Leu
		210					215					220				
	Ser	Thr	Ser	Glu	Lys	Ile	Phe	Arg	Phe	Gln	Asp	Thr	Gly	Leu	Leu	Leu
30	225					230					235					240
	Arg	Val	Leu	Gly	Ser	Leu	Phe	Leu	Gly	Gly	Ile	Leu	Ala	Phe	Gly	Leu
					245					250					255	
	G1y	Phe	Ser	Glu	Phe	Leu	Leu	Val	Ser	Arg	Thr	Ser	Ser	Leu	Thr	Leu
				260					265					270		
35	Ser	Ile		Gly	Ile	Phe	Lys		Val	Cys	Thr	Leu	Leu	Leu	Ala	Ala
			275					280					285			
	His		Leu	Gly	Asp	Gln		Ser	Leu	Leu	Asn	Trp	Leu	Gly	Phe	Ala
		290					295					300				

WO 98/55508

101

Leu Cys Leu Ser Gly Ile Ser Leu His Val Ala Leu Lys Ala Leu His 305 Ser Arg Gly Asp Gly Gly Pro Lys Ala Leu Lys Gly Leu Gly Ser Ser Pro Asp Leu Glu Leu Leu Arg Ser Ser Gln Arg Glu Glu Gly Asp 345 Asn Glu Glu Glu Tyr Phe Val Ala Gln Gly Gln Gln 355 360 365 10 (2) INFORMATION FOR SEQ ID NO: 15: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 226 (B) TYPE: Amino acid 15 (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No (vi) ORIGINAL SOURCE: 20 (A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10429 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15: 25 Met Pro Thr Thr Lys Lys Thr Leu Met Phe Leu Ser Ser Phe Phe Thr Ser Leu Gly Ser Phe Ile Val Ile Cys Ser Ile Leu Gly Thr Gln Ala 25 Trp Ile Thr Ser Thr Ile Ala Val Arg Asp Ser Ala Ser Asn Gly Ser 40 Ile Phe Ile Thr Tyr Gly Leu Phe Arg Gly Glu Ser Ser Glu Glu Leu 55 60 Ser His Gly Leu Ala Glu Pro Lys Lys Phe Ala Val Leu Glu Ile 35 65 70 Leu Asn Asn Ser Ser Gln Lys Thr Leu His Ser Val Thr Ile Leu Phe Leu Val Leu Ser Leu Ile Thr Ser Leu Leu Ser Ser Gly Phe Thr Phe

102

100 105 110 Tyr Asn Ser Ile Ser Asn Pro Tyr Gln Thr Phe Leu Gly Pro Thr Gly 115 120 Val Tyr Thr Trp Asn Gly Leu Gly Ala Ser Phe Val Phe Val Thr Met 5 135 140 Ile Leu Phe Val Ala Asn Thr Gln Ser Asn Gln Leu Ser Glu Glu Leu 145 150 155 Phe Gln Met Leu Tyr Pro Ala Thr Thr Ser Lys Gly Thr Thr His Ser 165 170 10 Tyr Gly Tyr Ser Phe Trp Leu Ile Leu Leu Val Ile Leu Leu Asn Ile 180 185 Val Thr Val Thr Ile Ile Ile Phe Tyr Gln Lys Ala Arg Tyr Gln Arg 200 Lys Gln Glu Gln Arg Lys Pro Met Glu Tyr Ala Pro Arg Asp Gly Ile 15 215 220 Leu Phe 225 20 (2) INFORMATION FOR SEQ ID NO: 16: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 129 (B) TYPE: Amino acid (D) TOPOLOGY: Linear 25 (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens 30 (B) CELL KIND: Liver (D) CLONE NAME: HP10432 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16: 35 Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly

103

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys 35 40 Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys 55 Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro .70 75 Ile Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser 85 90 Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Arg Glu Lys Phe Thr Thr 10 105 Pro Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu Ile 115 120 125 G1n 15 (2) INFORMATION FOR SEQ ID NO: 17: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 163 20 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Liver (D) CLONE NAME: HP10433 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17: Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly Ala Val Gly Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Arg Gly Leu Gln Val 35 20 25 30 Ala Leu Glu Glu Phe His Lys His Pro Pro Val Gln Trp Ala Phe Gln 40

Glu Thr Ser Val Glu Ser Ala Val Asp Thr Pro Phe Pro Ala Gly Ile

104

50 55 60 Phe Val Arg Leu Glu Phe Lys Leu Gln Gln Thr Ser Cys Arg Lys Arg 65 70 Asp Trp Lys Lys Pro Glu Cys Lys Val Arg Pro Asn Gly Arg Lys Arg 5 90 Lys Cys Leu Ala Cys Ile Lys Leu Gly Ser Glu Asp Lys Val Leu Gly 100 105 110 Arg Leu Val His Cys Pro Ile Glu Thr Gln Val Leu Arg Glu Ala Glu 120 10 Glu His Gln Glu Thr Gln Cys Leu Arg Val Gln Arg Ala Gly Glu Asp 130 135 Pro His Ser Phe Tyr Phe Pro Gly Gln Phe Ala Phe Ser Lys Ala Leu 150 155 Pro Arg Ser 15 (2) INFORMATION FOR SEQ ID NO: 18: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 193 20 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10480 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18: Met Ile Arg Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro 10 Leu Leu Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly 35 20 Arg Gly Trp Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp 40

Trp Lys Cys Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly

		50					55					60					
	Cys	Gln	Ser	Leu	Met	Glu	Tyr	Ala	Trp	Gly	Arg	Ala	Ala	Ala	Ala	Met	
	65					70					75					80	
	Leu	Phe	Cys	Gly	Phe	Ile	Ile	Leu	Val	Ile	Cys	Phe	Ile	Leu	Ser	Phe	
5					85					90					95		
	Phe	Ala	Leu	Cys	Gly	Pro	Gln	Met	Leu	Val	Phe	Leu	Arg	Val	Ile	Gly	
				100					105					110			
	Gly	Leu		Ala	Leu	Ala	Ala	Val	Phe	Gln	Ile	Ile	Ser	Leu	Va1	Ile	
			115					120					125				
10	Tyr		Val	Lys	Tyr	Thr		Thr	Phe	Thr	Leu	His	Ala	Asn	Arg	Ala	
		130	_		_		135					140					
		Thr	Tyr	Ile	Tyr		Trp	Ala	Tyr	Gly		Gly	Trp	Ala	Ala		
	145	T1.	7	71.	0.1	150					155	_		_	_	160	
15	116	TIE	Leu	11e	165	Cys	ALA	rne	Pne	170	Cys	Cys	Leu	Pro	Asn	Tyr	
.	Glu	Asn	Aen	T.eu		G1 v	Acn	Δ1 n	Ivo		۸	Ψ	Dho	Ф	175 Thr	50=	
		пор	nap	180	Deu	Gly	Vali	nia	185	PLO	Arg	lyr	rne	190	1111	ser	
	Ala			200					103					190			
20																	
	(2)	INFO	RMA	NOI	FOR	SEQ	ID N	io: 1	.9:				٠				
		(i	.) SI	EQUEN	ICE C	HARA	CTER	RISTI	CS:								
				(A)	LENG	TH:	1146	;									
				(B)	TYPE	: Nu	clei	.c ac	id								
25				(C)	STRA	NDED	NESS	: Do	uble	:							
				(D)	TOPO	LOGY	: Li	.near									
		(i	i) S	EQUE	NCE	KIND	: cI	NA t	o mR	.NA							
		(v	·i) (RIGI													
30								omo s	•	ns							
								inea									
				(D)	CLON	E NA	ME:	HP01	263								
		(POITE	MOR	DECO	D.T.D.M	TON	0.00	T D							
35		(х	.1) 5	EQUE	NCE	DESC	KIPT	TUN:	SEQ	ID	NO:	19:					
, ,	ATGG	Gጥርጥ -	ന വ	ייתייטטי	CCCC	ጥ ርር	<u> </u>	יר ייר ר	ል ጥር	ርጥ ላ ር	ጥርረ	መር መር	CTCC	CC 4	CC	TGTCT	60
															1	CCGAT	
																GCTAT	

	GTGCTGAGAC	TCAACCGAGT	GAACGACGCC	CAGGAATACA	GACGGGGTGG	CCTGGGATCT	240
	CTGTTCTATC	TTACACTGGA	TGTGCTAGAG	ACTGACTGCC	ATGTGCTCAG	AAAGAAGGCA	300
	TGGCAAGACT	GTGGAATGAG	GATATTTTT	GAATCAGTTT	ATGGTCAATG	CAAAGCAATA	360
	TTTTATATGA	ACAACCCAAG	TAGAGTTCTC	TATTTAGCTG	CTTATAACTG	TACTCTTCGC	420
5	CCAGTTTCAA	AAAAAAGAT	TTACATGACG	TGCCCTGACT	GCCCAAGCTC	CATACCCACT	480
	GACTCTTCCA	ATCACCAAGT	GCTGGAGGCT	GCCACCGAGT	CTCTTGCGAA	ATACAACAAT	540
	GAGAACACAT	CCAAGCAGTA	TTCTCTCTTC	AAAGTCACCA	GGGCTTCTAG	CCAGTGGGTG	600
	GTCGGCCCTT	CTTACTTTGT	GGAATACTTA	ATTAAAGAAT	CACCATGTAC	TAAATCCCAG	660
	GCCAGCAGCT	GTTCACTTCA	GTCCTCCGAC	TCTGTGCCTG	TTGGTCTTTG	CAAAGGTTCT	720
10	CTGACTCGAA	CACACTGGGA	AAAGTTTGTC	TCTGTGACTT	GTGACTTCTT	TGAATCACAG	780
	GCTCCAGCCA	CTGGAAGTGA	AAACTCTGCT	GTTAACCAGA	AACCTACAAA	CCTTCCCAAG	840
	GTGGAAGAAT	CCCAGCAGAA	AAACACCCCC	CCAACAGACT	CCCCCTCCAA	AGCTGGGCCA	900
	AGAGGATCTG	TCCAATATCT	TCCTGACTTG	GATGATAAAA	ATTCCCAGGA	AAAGGGCCCT	960
	CAGGAGGCCT	TTCCTGTGCA	TCTGGACCTA	ACCACGAATC	CCCAGGGAGA	AACCCTGGAT	1020
15	ATTTCCTTCC	TCTTCCTGGA	GCCTATGGAG	GAGAAGCTGG	TTGTCCTGCC	TTTCCCCAAA	1080
	GAAAAAGCAC	GCACTGCTGA	GTGCCCAGGG	CCAGCCCAGA	ATGCCAGCCC	TCTTGTCCTT	1140
	CCGCCA						1146

- 20 (2) INFORMATION FOR SEQ ID NO: 20:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 951
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 25 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP01299
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:
- AGGCAGGTGG TGAGCCACCT CCAAGACAAG TATGTCTTTA TCACGGGCTG TGACTCGGGC 120
 TTTGGGAACC TGCTGGCCAG ACAGCTGGAT GCACGAGGCT TGAGAGTGCT GGCTGCGTGT 180
 CTGACGGAGA AGGGGGCCGA GCAGCTGAGG GGCCAGACGT CTGACAGGCT GGAGACGGTG 240

107

	ACCCTGGATG	TTACCAAGAT	GGAGAGCATC	GCTGCAGCTA	CTCAGTGGGT	GAAGGAGCAT	300
	GTGGGGGACA	GAGGACTCTG	GGGACTGGTG	AACAATGCAG	GCATTCTTAC	ACCAATTACC	360
	TTATGTGAGT	GGCTGAACAC	TGAGGACTCT	ATGAATATGC	TCAAAGTGAA	CCTCATTGGT	420
	GTGATCCAGG	TGACCTTGAG	CATGCTTCCT	TTGGTGAGGA	GAGCACGGGG	AAGAATTGTC	480
5	AATGTCTCCA	GCATTCTGGG	AAGAGTTGCT	TTCTTTGTAG	GAGGCTACTG	TGTCTCCAAG	540
	TATGGAGTGG	AAGCCTTTTC	AGATATTCTG	AGGCGTGAGA	TTCAACATTT	TGGGGTGAAA	600
	ATCAGCATAG	TTGAACCTGG	CTACTTCAGA	ACGGGAATGA	CAAACATGAC	ACAGTCCTTA	660
	GAGCGAATGA	AGCAAAGTTG	GAAAGAAGCC	CCCAAGCATA	TTAAGGAGAC	CTATGGACAG	720
	CAGTATTTTG	ATGCCCTTTA	CAATATCATG	AAGGAAGGGC	TGTTGAATTG	TAGCACAAAC	780
10	CTGAACCTGG	TCACTGACTG	CATGGAACAT	GCTCTGACAT	CGGTGCATCC	GCGAACTCGA	840
	TATTCAGCTG	GCTGGGATGC	TAAATTTTTC	TTCATCCCTC	TATCTTATTT	ACCTACATCA	900
	CTGGCAGACT	ACATTTTGAC	TAGATCTTGG	CCCAAACCAG	CCCAGGCAGT	С	951

15 (2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 888
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 20 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP01347

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

30	ATGAGTGACT	CCAAGGAACC	AAGGGTGCAG	CAGCTGGGCC	TCCTGGGGTG	TCTTGGCCAT	60
	GGCGCCCTGG	TGCTGCAACT	CCTCTCCTTC	ATGCTCTTGG	CTGGGGTCCT	GGTGGCCATC	120
	CTTGTCCAAG	TGTCCAAGGT	CCCCAGCTCC	CTAAGTCAGG	AACAATCCGA	GCAAGACGCA	180
	ATCTACCAGA	ACCTGACCCA	GCTTAAAGCT	GCAGTGGGTG	AGCTCTCAGA	GAAATCCAAG	240
	CTGCAGGAGA	TCTACCAGGA	GCTGACCCAG	CTGAAGGCTG	CAGTGGGTGA	GTTGCCAGAG	300
35	AAATCCAAGC	TGCAGGAGAT	CTACCAGGAG	CTGACCCGGC	TGAAGGCTGC	AGTGGGTGAG	360
	TTGCCAGAGA	AATCCAAGCT	GCAGGAGATC	TACCAGGAGC	TGACCCGGCT	GAAGGCTGCA	420
	GTGGGTGAGT	TGCCAGAGAA	ATCCAAGCTG	CAGGAGATCT	ACCAGGAGCT	GACCCGGCTG	480
	AAGGCTGCAG	TGGGTGAGTT	GCCAGAGAAA	TCCAAGCTGC	AGGAGATCTA	CCAGGAGCTG	540

108

	ACGGAGCTGA	AGGCTGCAGT	GGGTGAGTTG	CCAGAGAAAT	CCAAGCTGCA	GGAGATCTAC	600
	CAGGAGCTGA	CCCAGCTGAA	GGCTGCAGTG	GGTGAGTTGC	CAGACCAGTC	CAAGCAGCAG	660
	CAAATCTATC	AAGAACTGAC	CGATTTGAAG	ACTGCATTTG	AACGCCTGTG	CCGCCACTGT	720
	CCCAAGGACT	GGACATTCTT	CCAAGGAAAC	TGTTACTTCA	TGTCTAACTC	CCAGCGGAAC	780
5	TGGCACGACT	CCGTCACCGC	CTGCCAGGAA	GTGAGGGCCC	AGCTCGTCGT	AATCAAAACT	840
	GCTGAGGAGC	AGCTTCCAGC	GGTACTGGAA	CAGTGGAGAA	CCCAACAA		888

(2) INFORMATION FOR SEQ ID NO: 22:

10 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 591

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

15 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

20 (D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

	ATGTGTACGG	GAAAATGTGC	CCGCTGTGTG	GGGCTCTCCC	TCATTACCCT	CTGCCTCGTC	60
25	TGCATTGTGG	CCAACGCCCT	CCTGCTGGTA	CCTAATGGGG	AGACCTCCTG	GACCAACACC	120
	AACCATCTCA	GCTTGCAAGT	CTGGCTCATG	GGCGGCTTCA	TTGGCGGGGG	CCTAATGGTA	180
	CTGTGTCCGG	GGATTGCAGC	CGTTCGGGCA	GGGGGCAAGG	GCTGCTGTGG	TGCTGGGTGC	240
	TGTGGAAACC	GCTGCAGGAT	GCTGCGCTCG	GTCTTCTCCT	CGGCGTTCGG	GGTGCTTGGT	300
	GCCATCTACT	GCCTCTCGGT	GTCTGGAGCT	GGGCTCCGAA	ATGGACCCAG	ATGCTTAATG	360
30	AACGGCGAGT	GGGGCTACCA	CTTCGAAGAC	ACCGCGGGAG	CTTACTTGCT	CAACCGCACT	420
	CTATGGGATC	GGTGCGAGGC	GCCCCTCGC	GTGGTCCCCT	GGAATGTGAC	GCTCTTCTCG	480
	CTGCTGGTGG	CCGCCTCCTG	CCTGGAGATA	GTACTGTGTG	GGATCCAGCT	GGTGAACGCG	540
	ACCATTGGTG	TCTTCTGCGG	CGATTGCAGG	AAAAAACAGG	ACACCCCTCA	С	591

35

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 663

109

		(B) TYPE: Nucleic acid	
		(C) STRANDEDNESS: Double	
		(D) TOPOLOGY: Linear	
	(ii)	SEQUENCE KIND: cDNA to mRNA	
5			
	(vi)	ORIGINAL SOURCE:	
		(A) ORGANISM: Homo sapiens	
		(B) CELL KIND: Stomach cancer	
		(D) CLONE NAME: HP01526	
10			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 23:	
	ATGGAGGCGG	GCGGCTTTCT GGACTCGCTC ATTTACGGAG CATGCGTGGT CTTCACCCT	T 60
	GGCATGTTCT	CCGCCGGCCT CTCGGACCTC AGGCACATGC GAATGACCCG GAGTGTGGA	.C 120
15	AACGTCCAGT	TCCTGCCCTT TCTCACCACG GAAGTCAACA ACCTGGGCTG GCTGAGTTA	T 180
	GGGGCTTTGA	AGGGAGACGG GATCCTCATC GTCGTCAACA CAGTGGGTGC TGCGCTTCA	.G 240
	ACCCTGTATA	TCTTGGCATA TCTGCATTAC TGCCCTCGGA AGCGTGTTGT GCTCCTACA	.G 300
	ACTGCAACCC	TGCTAGGGGT CCTTCTCCTG GGTTATGGCT ACTTTTGGCT CCTGGTACC	C 360
	AACCCTGAGG	CCCGGCTTCA GCAGTTGGGC CTCTTCTGCA GTGTCTTCAC CATCAGCAT	G 420
20	TACCTCTCAC	CACTGGCTGA CTTGGCTAAG GTGATTCAAA CTAAATCAAC CCAATGTCT	C 480
	TCCTACCCAC	TCACCATTGC TACCCTTCTC ACCTCTGCCT CCTGGTGCCT CTATGGGTT	T 540
	CGACTCAGAG	ATCCCTATAT CATGGTGTCC AACTTTCCAG GAATCGTCAC CAGCTTTAT	C 600
	CGCTTCTGGC	TTTTCTGGAA GTACCCCCAG GAGCAAGACA GGAACTACTG GCTCCTGCA	A 660
	ACC		663
25			
	(2) INFORMA	ATION FOR SEQ ID NO: 24:	
	(i) S	SEQUENCE CHARACTERISTICS:	
		(A) LENGTH: 753	
30		(B) TYPE: Nucleic acid	
		(C) STRANDEDNESS: Double	
		(D) TOPOLOGY: Linear	
	(ii)	SEQUENCE KIND: cDNA to mRNA	
35	(vi)	ORIGINAL SOURCE:	
		(A) ORGANISM: Homo sapiens	
		(B) CELL KIND: Stomach cancer	

(D) CLONE NAME: HP10230

110

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

	ATGTCGGACA	TCGGAGACTG	GTTCAGGAGC	ATCCCGGCGA	TCACGCGCTA	TTGGTTCGCC	60
	GCCACCGTCG	CCGTGCCCTT	GGTCGGCAAA	CTCGGCCTCA	TCAGCCCGGC	CTACCTCTTC	120
5	CTCTGGCCCG	AAGCCTTCCT	TTATCGCTTT	CAGATTTGGA	GGCCAATCAC	TGCCACCTTT	180
	TATTTCCCTG	TGGGTCCAGG	AACTGGATTT	CTTTATTTGG	TCAATTTATA	TTTCTTATAT	240
	CAGTATTCTA	CGCGACTTGA	AACAGGAGCT	TTTGATGGGA	GGCCAGCAGA	CTATTTATTC	300
	ATGCTCCTCT	TTAACTGGAT	TTGCATCGTG	ATTACTGGCT	TAGCAATGGA	TATGCAGTTG	360
	CTGATGATTC	CTCTGATCAT	GTCAGTACTT	TATGTCTGGG	CCCAGCTGAA	CAGAGACATG	420
10	ATTGTATCAT	TTTGGTTTGG	AACACGATTT	AAGGCCTGCT	ATTTACCCTG	GGTTATCCTT	480
	GGATTCAACT	ATATCATCGG	AGGCTCGGTA	ATCAATGAGC	TTATTGGAAA	TCTGGTTGGA	540
	CATCTTTATT	TTTTCCTAAT	GTTCAGATAC	CCAATGGACT	TGGGAGGAAG	AAATTTTCTA	600
	TCCACACCTC	AGTTTTTGTA	CCGCTGGCTG	CCCAGTAGGA	GAGGAGGAGT	ATCAGGATTT	660
	GGTGTGCCCC	CTGCTAGCAT	GAGGCGAGCT	GCTGATCAGA	ATGGCGGAGG	CGGGAGACAC	720
15	AACTGGGGCC	AGGGCTTTCG	ACTTGGAGAC	CAG			753

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

20

- (A) LENGTH: 318
- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: cDNA to mRNA

25

- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Epidermoid carcinoma
 - (C) CELL LINE: KB

30

(D) CLONE NAME: HP10389

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

	ATGGCGACTC	CCGGCCCTGT	GATTCCGGAG	GTCCCCTTTG	AACCATCGAA	GCCTCCAGTC	60
35	ATTGAGGGGC	TGAGCCCCAC	TGTTTACAGG	AATCCAGAGA	GTTTCAAGGA	AAAGTTCGTT	120
	CGCAAGACCC	GCGAGAACCC	GGTGGTACCC	ATAGGTTGCC	TGGCCACGGC	GGCCGCCCTC	180
	ACCTACGGCC	TCTACTCCTT	CCACCGGGGC	AACAGCCAGC	GCTCTCAGCT	CATGATGCGC	240
	ACCCGGATCG	CCGCCCAGGG	TTTCACGGTC	GCAGCCATCT	TGCTGGGTCT	GGCTGTCACT	300

111

318

GCTATGAAGT CTCGACCC

	(2) INFORMATION FOR SEQ ID NO: 26:	
5	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 234	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
10	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
15	(D) CLONE NAME: HP10408	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:	
	ATGGGGTCTG GGCTGCCCCT TGTCCTCCTC TTGACCCTCC TTGGCAGCTC ACATGGAACA	60
20	GGGCCGGGTA TGACTTTGCA ACTGAAGCTG AAGGAGTCTT TTCTGACAAA TTCCTCCTAT	120
	GAGTCCAGCT TCCTGGAATT GCTTGAAAAG CTCTGCCTCC TCCTCCATCT CCCTTCAGGG	180
	ACCAGCGTCA CCCTCCACCA TGCAAGATCT CAACACCATG TTGTCTGCAA CACA	234
25	(2) INFORMATION FOR SEQ ID NO: 27:	
23	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 942	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
30	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
35	(B) CELL KIND: Stomach cancer	

(D) CLONE NAME: HP10412

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

	ATGGTGGCGC	CTGTGTGGTA	CTTGGTAGCG	GCGGCTCTGC	TAGTCGGCTT	TATCCTCTTC	60
	CTGACTCGCA	GCCGGGGCCG	GGCGGCATCA	GCCGGCCAAG	AGCCACTGCA	CAATGAGGAG	120
	CTGGCAGGAG	CAGGCCGGGT	GGCCCAGCCT	GGGCCCCTGG	AGCCTGAGGA	GCCGAGAGCT	180
	GGAGGCAGGC	CTCGGCGCCG	GAGGGACCTG	GGCAGCCGCC	TACAGGCCCA	GCGTCGAGCC	240
5	CAGCGGGTGG	CCTGGGCAGA	AGCAGATGAG	AACGAGGAGG	AAGCTGTCAT	CCTAGCCCAG	300
	GAGGAGGAAG	GTGTCGAGAA	GCCAGCGGAA	ACTCACCTGT	CGGGGAAAAT	TGGAGCTAAG	360
	AAACTGCGGA	AGCTGGAGGA	GAAACAAGCG	CGAAAGGCCC	AGCGTGAGGC	AGAGGAGGCT	420
	GAACGTGAGG	AGCGGAAACG	ACTCGAGTCC	CAGCGCGAAG	CTGAGTGGAA	GAAGGAGGAG	480
	GAGCGGCTTC	GCCTGGAGGA	GGAGCAGAAG	GAGGAGGAGG	AGAGGAAGGC	CCGCGAGGAG	540
10	CAGGCCCAGC	GGGAGCATGA	GGAGTACCTG	AAACTGAAGG	AGGCCTTTGT	GGTGGAGGAG	600
	GAAGGCGTAG	GAGAGACCAT	GACTGAGGAA	CAGTCCCAGA	GCTTCCTGAC	AGAGTTCATC	660
	AACTACATCA	AGCAGTCCAA	GGTTGTGCTC	TTGGAAGACC	TGGCTTCCCA	GGTGGGCCTA	720
	CGCACTCAGG	ACACCATAAA	TCGCATCCAG	GACCTGCTGG	CTGAGGGGAC	TATAACAGGT	780
	GTGATTGACG	ACCGGGGCAA	GTTCATCTAC	ATAACCCCAG	AGGAACTGGC	CGCCGTGGCC	840
15	AACTTCATCC	GACAGCGGGG	CCGGGTGTCC	ATCGCCGAGC	TTGCCCAAGC	CAGCAACTCC	900
	CTCATCGCCT	GGGGCCGGGA	GTCCCCTGCC	CAAGCCCCAG	CC		942

(2) INFORMATION FOR SEQ ID NO: 28:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 585

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

25 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

30 (D) CLONE NAME: HP10413

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

	ATGGCTGCCG	AGGATGTGGT	GGCGACTGGC	GCCGACCCAA	GCGATCTGGA	GAGCGGCGGG	60
35	CTGCTGCATG	AGATTTTCAC	GTCGCCGCTC	AACCTGCTGC	TGCTTGGCCT	CTGCATCTTC	120
	CTGCTCTACA	AGATCGTGCG	CGGGGACCAG	CCGGCGGCCA	GCGGCGACAG	CGACGACGAC	180
	GAGCCGCCCC	CTCTGCCCCG	CCTCAAGCGG	CGCGACTTCA	CCCCGCCGA	GCTGCGGCGC	240
	TTCGACGGCG	TCCAGGACCC	GCGCATACTC	ATGGCCATCA	ACGCCAAGGT	GTTCGATGTG	300

113

	ACCAAAGGCC	GCAAATTCTA	CGGGCCCGAG	GGGCCGTATG	GGGTCTTTGC	TGGAAGAGAT	360
	GCATCCAGGG	GCCTTGCCAC	ATTTTGCCTG	GATAAGGAAG	CACTGAAGGA	TGAGTACGAT	420
	GACCTTTCTG	ACCTCACTGC	TGCCCAGCAG	GAGACTCTGA	GTGACTGGGA	GTCTCAGTTC	480
	ACTTTCAAGT	ATCATCACGT	GGGCAAACTG	CTGAAGGAGG	GGGAGGAGCC	CACTGTGTAC	540
5	TCAGATGAGG	AAGAACCAAA	AGATGAGAGT	GCCCGGAAAA	ATGAT		585

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 1386

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

15

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10415

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

ATGTTGGACT TCGCGATCTT CGCCGTTACC TTCTTGCTGG CGTTGGTGGG AGCCGTGCTC 60 TACCTCTATC CGGCTTCCAG ACAAGCTGCA GGAATTCCAG GGATTACTCC AACTGAAGAA 120 25 AAAGATGGTA ATCTTCCAGA TATTGTGAAT AGTGGAAGTT TGCATGAGTT CCTGGTTAAT 180 TTGCATGAGA GATATGGGCC TGTGGTCTCC TTCTGGTTTG GCAGGCGCCT CGTGGTTAGT 240 TTGGGCACTG TTGATGTACT GAAGCAGCAT ATCAATCCCA ATAAGACATT GGACCCTTTT 300 GAAACCATGC TGAAGTCATT ATTAAGGTAT CAATCTGGTG GTGGCAGTGT GAGTGAAAAC 360 CACATGAGGA AAAAATTGTA TGAAAATGGT GTGACTGATT CTCTGAAGAG TAACTTTGCC 420 30 CTCCTCCTAA AGCTTTCAGA AGAATTATTA GATAAATGGC TCTCCTACCC AGAGACCCAG 480 CACGTGCCCC TCAGCCAGCA TATGCTTGGT TTTGCTATGA AGTCTGTTAC ACAGATGGTA 540 ATGGGTAGTA CATTTGAAGA TGATCAGGAA GTCATTCGCT TCCAGAAGAA TCATGGCACA 600 GTTTGGTCTG AGATTGGAAA AGGCTTTCTA GATGGGTCAC TTGATAAAAA CATGACTCGG 660 AAAAAACAAT ATGAAGATGC CCTCATGCAA CTGGAGTCTG TTTTAAGGAA CATCATAAAA 720 35 GAACGAAAAG GAAGGAACTT CAGTCAACAT ATTTTCATTG ACTCCTTAGT ACAAGGGAAC 780 CTTAATGACC AACAGATCCT AGAAGACAGT ATGATATTTT CTCTGGCCAG TTGCATAATA ACTGCAAAAT TGTGTACCTG GGCAATCTGT TTTTTAACCA CCTCTGAAGA AGTTCAAAAA 900 AAATTATATG AAGAGATAAA CCAAGTTTTT GGAAATGGTC CTGTTACTCC AGAGAAAATT 960

114

	GAGCAGCTCA	GATATTGTCA	GCATGTGCTT	TGTGAAACTG	TTCGAACTGC	CAAACTGACT	1020
	CCAGTTTCTG	CCCAGCTTCA	AGATATTGAA	GGAAAAATTG	ACCGATTTAT	TATTCCTAGA	1080
	GAGACCCTCG	TCCTTTATGC	CCTTGGTGTG	GTACTTCAGG	ATCCTAATAC	TTGGCCATCT	1140
	CCACACAAGT	TTGATCCAGA	TCGGTTTGAT	GATGAATTAG	TAATGAAAAC	TTTTTCCTCA	1200
5	CTTGGATTCT	CAGGCACACA	GGAGTGTCCA	GAGTTGAGGT	TTGCATATAT	GGTGACCACA	1260
	GTACTTCTTA	GTGTATTGGT	GAAGAGACTG	CACCTACTTT	CTGTGGAGGG	ACAGGTTATT	1320
	GAAACAAAGT	ATGAACTGGT	AACATCATCA	AGGGAAGAAG	CTTGGATCAC	TGTCTCAAAG	1380
	AGATAT						1386
10							
	(2) INFORM	ATION FOR SI	EQ ID NO: 30	0:		•	
	(i)	SEQUENCE CHA	ARACTERISTIC	CS:			
		(A) LENGTH	H: 741				
		(B) TYPE:	Nucleic ac	id			
15		(C) STRANI	DEDNESS: Dot	ıble			
		(D) TOPOLO	OGY: Linear				
	(ii)	SEQUENCE KI	IND: cDNA to	mRNA			
	(vi)	ORIGINAL SO	OURCE:				
20		(A) ORGANI	ISM: Homo sa	spiens			
		(B) CELL F	KIND: Stomac	ch cancer			
		(D) CLONE	NAME: HP104	19	•		
	(xi)	SEQUENCE DE	ESCRIPTION:	SEQ ID NO:	30:		
25							
	ATGGGGGCTG	CGGTGTTTTT	CGGCTGCACT	TTCGTCGCGT	TCGGCCCGGC	CTTCGCGCTT	60
	TTCTTGATCA	CTGTGGCTGG	GGACCCGCTT	CGCGTTATCA	TCCTGGTCGC	AGGGGCATTT	120
	TTCTGGCTGG	TCTCCCTGCT	CCTGGCCTCT	GTGGTCTGGT	TCATCTTGGT	CCATGTGACC	180
	GACCGGTCAG	ATGCCCGGCT	CCAGTACGGC	CTCCTGATTT	TTGGTGCTGC	TGTCTCTGTC	240
30	CTTCTACAGG	AGGTGTTCCG	CTTTGCCTAC	TACAAGCTGC	TTAAGAAGGC	AGATGAGGGG	300
		TGAGTGAGGA					360
	TCTGGTCTCT	CCTTCGGTAT	CATCAGTGGT	GTCTTCTCTG	TTATCAATAT	TTTGGCTGAT	420
	GCACTTGGGC	CAGGTGTGGT	TGGGATCCAT	GGAGACTCAC	CCTATTACTT	CCTGACTTCA	480
		CAGCAGCCAT					540
35		GGAGACGGTA					600
		CATTCCTGAA					660
	ACTGTTTCCA	TGGGGCTCTG	GGCCTTCATC	ACAGCTGGAG	GGTCCCTCCG	AAGTATTCAG	720

741

CGCAGCCTCT TGTGTAAGGA C

	(2) INFORMATION FOR SEQ ID NO: 31:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 339	
5	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
10	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10424	
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:	
	ATGAACTTCT ATTTACTCCT AGCGAGCAGC ATTCTGTGTG CCTTGATTGT CTTCTGGAAA	60
	TATCGCCGCT TTCAGAGAAA CACTGGCGAA ATGTCATCAA ATTCAACTGC TCTTGCACTA	120
	GTGAGACCCT CTTCTTCTGG GTTAATTAAC AGCAATACAG ACAACAATCT TGCAGTCTAC	180
20	GACCTCTCTC GGGATATTTT AAATAATTTC CCACACTCAA TAGCCAGGCA GAAGCGAATA	240
	TTGGTAAACC TCAGTATGGT GGAAAACAAG CTGGTTGAAC TGGAACATAC TCTACTTAGC	300
	AAGGGTTTCA GAGGTGCATC ACCTCACCGG AAATCCACC	339
25	(2) INFORMATION FOR SEQ ID NO: 32:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1095	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
30	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
25	(A) ORGANISM: Homo sapiens	
35	(B) CELL KIND: Epidermoid carcinoma	

(C) CELL LINE: KB

(D) CLONE NAME: HP10428

116

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

	ATGGGGAGGT	GGGCCCTCGA	TGTGGCCTTT	TTGTGGAAGG	CGGTGTTGAC	CCTGGGGCTG	60
	GTGCTTCTCT	ACTACTGCTT	CTCCATCGGC	ATCACCTTCT	ACAACAAGTG	GCTGACAAAG	120
5	AGCTTCCATT	TCCCCCTCTT	CATGACGATG	CTGCACCTGG	CCGTGATCTT	CCTCTTCTCC	180
	GCCCTGTCCA	GGGCGCTGGT	TCAGTGCTCC	AGCCACAGGG	CCCGTGTGGT	GCTGAGCTGG	240
	GCCGACTACC	TCAGAAGAGT	GGCTCCCACA	GCTCTGGCGA	CGGCGCTTGA	CGTGGGCTTG	300
	TCCAACTGGA	GCTTCCTGTA	TGTCACCGTC	TCGCTGTACA	CAATGACCAA	ATCCTCAGCT	360
	GTCCTCTTCA	TCTTGATCTT	CTCTCTGATC	TTCAAGCTGG	AGGAGCTGCG	CGCGGCACTG	420
10	GTCCTGGTGG	TCCTCCTCAT	CGCCGGGGGT	CTCTTCATGT	TCACCTACAA	GTCCACACAG	480
	TTCAACGTGG	AGGGCTTCGC	CTTGGTGCTG	GGGGCCTCGT	TCATCGGTGG	CATTCGCTGG	540
•	ACCCTCACCC	AGATGCTCCT	GCAGAAGGCT	GAACTCGGCC	TCCAGAATCC	CATCGACACC	600
	ATGTTCCACC	TGCAGCCACT	CATGTTCCTG	GGGCTCTTCC	CTCTCTTTGC	TGTATTTGAA	660
	GGTCTCCATT	TGTCCACATC	TGAGAAAATC	TTCCGTTTCC	AGGACACAGG	GCTGCTCCTG	720
15	CGGGTACTTG	GGAGCCTCTT	CCTTGGCGGG	ATTCTCGCCT	TTGGTTTGGG	CTTCTCTGAG	780
	TTCCTCCTGG	TCTCCAGAAC	CTCCAGCCTC	ACTCTCTCCA	TTGCCGGCAT	TTTTAAGGAA	840
	GTCTGCACTT	TGCTGTTGGC	AGCTCATCTG	CTGGGCGATC	AGATCAGCCT	CCTGAACTGG	900
	CTGGGCTTCG	CCCTCTGCCT	CTCGGGAATA	TCCCTCCACG	TTGCCCTCAA	AGCCCTGCAT	960
	TCCAGAGGTG	ATGGTGGCCC	CAAGGCCTTG	AAGGGGCTGG	GCTCCAGCCC	CGACCTGGAG	1020
20	CTGCTGCTCC	GGAGCAGCCA	GCGGGAGGAA	GGTGACAATG	AGGAGGAGGA	GTACTTTGTG	1080
	GCCCAGGGGC	AGCAG					1095

(2) INFORMATION FOR SEQ ID NO: 33:

- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 678
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
- 30 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- 35 (D) CLONE NAME: HP10429
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

	ATGCCTACCA	CAAAGAAGAC A	TTGATGTTC	TTATCAAGCT	TTTTCACCAG	CCTTGGGTCC	60
	TTCATTGTAA	TTTGCTCTAT T	CTTGGGACA	CAAGCATGGA	TCACCAGTAC	AATTGCTGTT	120
	AGAGACTCTG	CTTCAAATGG G	AGCATTTTC	ATCACTTACG	GACTTTTTCG	TGGGGAGAGT	180
	AGTGAAGAAT	TGAGTCACGG A	CTTGCAGAA	CCAAAGAAAA	AGTTTGCAGT	TTTAGAGATA	240
5	CTGAATAATT	CTTCCCAAAA A	ACTCTGCAT	TCGGTGACTA	TCCTGTTCCT	GGTCCTGAGT	300
	TTGATCACGT	CGCTGCTGAG C	TCTGGGTTT	ACCTTCTACA	ACAGCATCAG	CAACCCTTAC	360
	CAGACATTCC	TGGGGCCGAC G	GGGGTGTAC	ACCTGGAACG	GGCTCGGTGC	ATCCTTCGTT	420
	TTTGTGACCA	TGATACTGTT TO	GTGGCGAAC	ACGCAGTCCA	ACCAACTCTC	CGAAGAGTTG	480
	TTCCAAATGC	TTTACCCGGC A	ACCACCAGT	AAAGGAACGA	CCCACAGTTA	CGGATACTCG	540
10	TTCTGGCTCA	TACTGCTCGT CA	ATTCTTCTA	AATATAGTCA	CTGTAACCAT	CATCATTTTC	600
	TACCAGAAGG	CCAGATACCA G	CGGAAGCAG	GAGCAGAGAA	AGCCAATGGA	ATATGCTCCA	660
	AGGGACGGAA	TTTTATTC					678
15	(2) INFORMA	TION FOR SEQ	ID NO: 34	:			
	(i) S	EQUENCE CHARA	ACTERISTIC	S:			
		(A) LENGTH:	387				
		(B) TYPE: No	ucleic aci	.d			
		(C) STRANDEI	DNESS: Dou	ble			
20		(D) TOPOLOGY	Y: Linear				
	(ii)	SEQUENCE KINI	D: cDNA to	mRNA			
	(vi)	ORIGINAL SOUR	RCE:				
		(A) ORGANISM	1: Homo sa	piens			
25		(B) CELL KIN	ND: Liver				
		(D) CLONE NA	ME: HP104	32			
	(xi)	SEQUENCE DESC	CRIPTION:	SEQ ID NO:	34:		
30							
	ATGGCTCGGG	SCTCGCTGCG CC	GGTTGCTG	CGGCTCCTCG	TGCTGGGGCT	CTGGCTGGCG	60
	TTGCTGCGCT	CCGTGGCCGG GG	GAGCAAGCG	CCAGGCACCG	CCCCCTGCTC	CCGCGGCAGC	120
	TCCTGGAGCG	CGGACCTGGA CA	AGTGCATG	GACTGCGCGT	CTTGCAGGGC	GCGACCGCAC	180
	AGCGACTTCT	SCCTGGGCTG CG	CTGCAGCA	CCTCCTGCCC	CCTTCCGGCT	GCTTTGGCCC	240
35	ATCCTTGGGG (CCCTCTGAG CC	TGACCTTC	GTGCTGGGGC	TGCTTTCTGG	CTTTTTGGTC	300
	TGGAGACGAT	CCGCAGGAG AG	AGAAGTTC A	ACCACCCCA	TAGAGGAGAC	CGGCGGAGAG	360
	GGCTGCCCAG	TGTGGCGCT GA	TCCAG			•	387

WO 98/55508

PCT/JP98/02445

	(2) INFORMATION FOR SEQ ID NO: 35:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 489	
	(B) TYPE: Nucleic acid	
5	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
10	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Liver	
	(D) CLONE NAME: HP10433	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:	
15		
	ATGCGACGGC TGCTGATCCC TCTGGCCCTG TGGCTGGGCG CGGTGGGCGT GGGCGTCGCC	60
	GAGCTCACGG AAGCCCAGCG CCGGGGCCTG CAGGTGGCCC TGGAGGAATT TCACAAGCAC	120
	CCGCCCGTGC AGTGGGCCTT CCAGGAGACC AGTGTGGAGA GCGCCGTGGA CACGCCCTTC	180
	CCAGCTGGAA TATTTGTGAG GCTGGAATTT AAGCTGCAGC AGACAAGCTG CCGGAAGAGG	240
20	GACTGGAAGA AACCCGAGTG CAAAGTCAGG CCCAATGGGA GGAAACGGAA ATGCCTGGCC	300
	TGCATCAAAC TGGGCTCTGA GGACAAAGTT CTGGGCCGGT TGGTCCACTG CCCCATAGAG	360
	ACCCAAGTTC TGCGGGAGGC TGAGGAGCAC CAGGAGACCC AGTGCCTCAG GGTGCAGCGG	420
	GCTGGTGAGG ACCCCCACAG CTTCTACTTC CCTGGACAGT TCGCCTTCTC CAAGGCCCTG	480
	CCCCGCAGC	489
25		
	(2) INFORMATION FOR SEQ ID NO: 36:	
	(1) SEQUENCE CHARACTERISTICS:	
20	(A) LENGTH: 579	
30	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
35	(vi) ORIGINAL SOURCE:	
J J	(VI) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10480	
	(D) ODONE NAME: NEIVAAU	

119

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

	ATGATCCGCT GCGGCCTGGC CTGCGAGCGC TGCCGCTGGA TCCTGCCCCT GCTCCTACTC	60
	AGCGCCATCG CCTTCGACAT CATCGCGCTG GCCGGCCGCG GCTGGTTGCA GTCTAGCGAC	120
5	CACGGCCAGA CGTCCTCGCT GTGGTGGAAA TGCTCCCAAG AGGGCGGCGG CAGCGGGTCC	180
	TACGAGGAGG GCTGTCAGAG CCTCATGGAG TACGCGTGGG GTAGAGCAGC GGCTGCCATG	240
	CTCTTCTGTG GCTTCATCAT CCTGGTGATC TGTTTCATCC TCTCCTTCTT CGCCCTCTGT	300
	GGACCCCAGA TGCTTGTCTT CCTGAGAGTG ATTGGAGGTC TCCTTGCCTT GGCTGCTGTG	360
	TTCCAGATCA TCTCCCTGGT AATTTACCCC GTGAAGTACA CCCAGACCTT CACCCTTCAT	420
10	GCCAACCGTG CTGTCACTTA CATCTATAAC TGGGCCTACG GCTTTGGGTG GGCAGCCACG	480
	ATTATCCTGA TCGGCTGTGC CTTCTTCTTC TGCTGCCTCC CCAACTACGA AGATGACCTT	540
	CTGGGCAATG CCAAGCCCAG GTACTTCTAC ACATCTGCC	579
15	(2) INFORMATION FOR SEQ ID NO: 37:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1502	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
20	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
25	(B) CELL KIND: Liver	
	(D) CLONE NAME: HP01263	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
30	(B) EXISTENCE POSITION: 37 1185	
	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:	
35	ACAAACTGAC CCATCCTGGG CCTTGTTCTC CACAGA ATG GGT CTG CTC CTT CCC	54
	Met Gly Leu Leu Pro	•
	1 5	

CTG GCA CTC TGC ATC CTA GTC CTG TGC TGC GGA GCA ATG TCT CCA CCC 102

	Leu	Ala	Leu	Cys	Ile	Leu	Val	Leu	Cys	Cys	Gly	Ala	Met	Ser	Pro	Pro	
				10					15					20			
	CAG	CTG	GCC	CTC	AAC	CCC	TCG	GCT	CTG	CTC	TCC	CGG	GGC	TGC	AAT	GAC	150
	Gln	Leu	Ala	Leu	Asn	Pro	Ser	Ala	Leu	Leu	Ser	Arg	Gly	Cys	Asn	Asp	
5			25					30					35				
	TCC	GAT	GTG	CTG	GCA	GTT	GCA	GGC	TTT	GCC	CTG	CGG	GAT	ATT	AAC	AAA	198
	Ser	Asp	Val	Leu	Ala	Val	Ala	Gly	Phe	Ala	Leu	Arg	Asp	Ile	Asn	Lys	
		40					45					50					
	GAC	AGA	AAG	GAT	GGC	TAT	GTG	CTG	AGA	CTC	AAC	CGA	GTG	AAC	GAC	GCC	246
10	Asp	Arg	Lys	Asp	Gly	Tyr	Val	Leu	Arg	Leu	Asn	Arg	Val	Asn	Asp	Ala	
	55					60					65					70	
	CAG	GAA	TAC	AGA	CGG	GGT	GGC	CTG	GGA	TCT	CTG	TTC	TAT	CTT	ACA	CTG	294
	Gln	Glu	Tyr	Arg	Arg	Gly	Gly	Leu	Gly	Ser	Leu	Phe	Tyr	Leu	Thr	Leu	
					75					80	•				85	٠	
15	GAT	GTG	CTA	GAG	ACT	GAC	TGC	CAT	GTG	CTC	AGA	AAG	AAG	GCA	TGG	CAA	342
	Asp	Val	Leu	Glu	Thr	Asp	Cys	His	Val	Leu	Arg	Lys	Lys	Ala	Trp	Gln	
				90					95					100			
	GAC	TGT	GGA	ATG	AGG	ATA	TTT	TTT	GAA	TCA	GTT	TAT	GGT	CAA	TGC	AAA	390
	Asp	Cys	Gly	Met	Arg	Ile	Phe	Phe	Glu	Ser	Val	Tyr	Gly	Gln	Cys	Lys	
20			105					110					115				
			TTT														438
	Ala		Phe	Tyr	Met	Asn	Asn	Pro	Ser	Arg	Val	Leu	Tyr	Leu	Ala	Ala	
		120					125					130					
			TGT														486
25		Asn	Cys	Thr	Leu		Pro	Val	Ser	Lys	Lys	Lys	Ile	Tyr	Met	Thr	
	135					140					145					150	
	TGC	CCT	GAC	TGC	CCA	AGC	TCC	ATA	CCC	ACT	GAC	TCT	TCC	AAT	CAC	CAA	534
	Cys	Pro	Asp	Cys		Ser	Ser	Ile	Pro	Thr	Asp	Ser	Ser	Asn	His	Gln	
					155					160					165		
30			GAG														582
	Val	Leu	Glu		Ala	Thr	Glu	Ser	Leu	Ala	Lys	Tyr	Asn	Asn	Glu	Asn	
				170					175					180			
			AAG														630
	Thr	Ser	Lys	Gln	Tyr	Ser	Leu	Phe	Lys	Val	Thr	Arg	Ala	Ser	Ser	G1n	
35	mo-	05-	185		_=. /	-4	_*.	190					195				
			GTC														678
	Trp		Val	Gly	Pro	Ser		Phe	Val	Glu	Tyr		Ile	Lys	Glu	Ser	
		200					205					210					

	CCA	TGT	ACT	AAA	TCC	CAG	GCC	AGC	AGC	TGT	TCA	CTT	CAG	TCC	TCC	GAC	726
	Pro	Cys	Thr	Lys	Ser	Gln	Ala	Ser	Ser	Cys	Ser	Leu	Gln	Ser	Ser	Asp	
	215					220					225					230	
	TCT	GTG	CCT	GTT	GGT	CTT	TGC	AAA	GGT	TCT	CTG	ACT	CGA	ACA	CAC	TGG	774
5	Ser	Val	Pro	Va1	Gly	Leu	Cys	Lys	Gly	Ser	Leu	Thr	Arg	Thr	His	Trp	
					235					240					245		
	GAA	AAG	TTT	GTC	TCT	GTG	ACT	TGT	GAC	TTC	TTT	GAA	TCA	CAG	GCT	CCA	822
	Glu	Lys	Phe	Val	Ser	Val	Thr	Cys	Asp	Phe	Phe	Glu	Ser	Gln	Ala	Pro	
				250					255					260			
10	GCC	ACT	GGA	AGT	GAA	AAC	TCT	GCT	GTT	AAC	CAG	AAA	CCT	ACA	AAC	CTT	870
	Ala	Thr	Gly	Ser	Glu	Asn	Ser	Ala	Val	Asn	Gln	Lys	Pro	Thr	Asn	Leu	
			265					270					275				
	CCC	AAG	GTG	GAA	GAA	TCC	CAG	CAG	AAA	AAC	ACC	CCC	CCA	ACA	GAC	TCC	918
	Pro	Lys	Val	Glu	Glu	Ser	Gln	Gln	Lys	Asn	Thr	Pro	Pro	Thr	Asp	Ser	
15		280					285					290					
	CCC	TCC	AAA	GCT	GGG	CCA	AGA	GGA	TCT	GTC	CAA	TAT	CTT	CCT	GAC	TTG	966
	Pro	Ser	Lys	Ala	Gly	Pro	Arg	Gly	Ser	Val	Gln	Tyr	Leu	Pro	Asp	Leu	
	295					300					305					310	
	GAT	GAT	AAA	AAT	TCC	CAG	GAA	AAG	GGC	CCT	CAG	GAG	GCC	TTT	CCT	GTG	1014
20	Asp	Asp	Lys	Asn	Ser	Gln	Glu	Lys	Gly	Pro	Gln	Glu	Ala	Phe	Pro	Val	
					315					320					325		
	CAT	CTG	GAC	CTA	ACC	ACG	AAT	CCC	CAG	GGA	GAA	ACC	CTG	GAT	ATT	TCC	1062
	His	Leu	Asp	Leu	Thr	Thr	Asn	Pro	Gln	Gly	Glu	Thr	Leu	Asp	Ile	Ser	
				330					335					340			
25	TTC	CTC	TTC	CTG	GAG	CCT	ATG	GAG	GAG	AAG	CTG	GTT	GTC	CTG	CCT	TTC	1110
	Phe	Leu	Phe	Leu	Glu	Pro	Met	Glu	Glu	Lys	Leu	Val	Val	Leu	Pro	Phe	
			345					350					355				
													CCA				1158
	Pro		Glu	Lys	Ala	Arg	Thr	Ala	Glu	Cys	Pro	Gly	Pro	Ala	Gln	Asn	
30		360					365					370					
									TGAG	AATC	AC A	CAGA	GTCT	T CT	GTAG	GG	1210
		Ser	Pro	Leu	Val	Leu	Pro	Pro									
	375					380											
																GTGCA	1270
35																TGACT	1330
																ACTGC	1390
																ATGCC	1450
	TCTC	TATT	GT C	TTCA	.GCCA	C TC	ACTT	'ATAA	AGA	TACT	TAT	CTTT	TCAG	CAG	T		1502

	(2) INFORMATION	1 FOR 3EQ 1D NO: 38:	
	(i) SEQUE	ENCE CHARACTERISTICS:	
	(A)) LENGTH: 1349	
5	(B)) TYPE: Nucleic acid	
	(C)	STRANDEDNESS: Double	
	(D)	TOPOLOGY: Linear	
	(ii) SEQU	JENCE KIND: cDNA to mRNA	
10	(vi) ORIG	GINAL SOURCE:	
	(A)	ORGANISM: Homo sapiens	
	(B)	CELL KIND: Liver	
	(D)	CLONE NAME: HP01299	
15			
	(ix) SEQU	JENCE CHARACTERISTICS:	
	(A)	CHARACTERIZATION CODE: CDS	
	(B)	EXISTENCE POSITION: 111 1064	
	(C)	CHARACTERIZATION METHOD: E	
20			
	(xi) SEQU	TENCE DESCRIPTION: SEQ ID NO: 38:	
	AGCAGTTGGG GCAG	GAGGAA GCCGACTGCT GCCTGGTCTG CAAAGAAGTC CTTTCAAGTC	60
	TCTAGGACTG GACT	CTTCCT AAGCAAGTCC GAGAAGGAAG CACCCTCACT ATG TGG	116
25		Met Trp	
		1	
		GCC TTC GTG GGC CTG TAC TAC CTT CTG CAC TGG TAC	
	164		
		Ala Phe Val Gly Leu Tyr Tyr Leu Leu His Trp Tyr	
30	5	10 15	
		GTG GTG AGC CAC CTC CAA GAC AAG TAT GTC TTT ATC	212
		Val Val Ser His Leu Gln Asp Lys Tyr Val Phe Ile	
	20	25 30	
		TCG GGC TTT GGG AAC CTG CTG GCC AGA CAG CTG GAT	260
35		Ser Gly Phe Gly Asn Leu Leu Ala Arg Gln Leu Asp	
	35	40 45 50	
		AGA GTG CTG GCT GCG TGT CTG ACG GAG AAG GGG GCC	308
	Ala Arg Gly Leu	Arg Val Leu Ala Ala Cys Leu Thr Glu Lys Gly Ala	

					55					60)				65	i	
	GAG	CAG	CTG	AGG	GGC	CAG	ACG	TCT	GAC	AGG	CTG	GAG	ACG	GTG	ACC	CTG	356
	Glu	Gln	Leu	Arg	Gly	Gln	Thr	Ser	Asp	Arg	Leu	Glu	Thr	Val	Thr	Leu	
				70					75					80			
5	GAT	GTT	ACC	AAG	ATG	GAG	AGC	ATC	GCT	GCA	GCT	ACT	CAG	TGG	GTG	AAG	404
	Asp	Val	Thr	Lys	Met	Glu	Ser	Ile	Ala	Ala	Ala	Thr	Gln	Trp	Val	Lys	
			85					90					95				
	GAG	CAT	GTG	GGG	GAC	AGA	GGA	CTC	TGG	GGA	CTG	GTG	AAC	AAT	GCA	GGC	452
	Glu	His	Val	Gly	Asp	Arg	Gly	Leu	Trp	Gly	Leu	Val	Asn	Asn	Ala	Gly	
10		100	•				105					110					
	ATT	CTT	ACA	CCA	ATT	ACC	TTA	TGT	GAG	TGG	CTG	AAC	ACT	GAG	GAC	TCT	500
	Ile	Leu	Thr	Pro	Ile	Thr	Leu	Cys	Glu	Trp	Leu	Asn	Thr	Glu	Asp	Ser	
	115					120					125					130	
	ATG	AAT	ATG	CTC	AAA	GTG	AAC	CTC	ATT	GGT	GTG	ATC	CAG	GTG	ACC	TTG	548
15	Met	Asn	Met	Leu	Lys	Val	Asn	Leu	Ile	Gly	Val	Ile	Gln	Val	Thr	Leu	
					135					140					145		
	AGC	ATG	CTT	CCT	TTG	GTG	AGG	AGA	GCA	CGG	GGA	AGA	ATT	GTC	AAT	GTC	596
	Ser	Met	Leu	Pro	Leu	Val	Arg	Arg	Ala	Arg	Gly	Arg	Ile	Val	Asn	Val	
				150					155					160			
20	TCC	AGC	ATT	CTG	GGA	AGA	GTT	GCT	TTC	TTT	GTA	GGA	GGC	TAC	TGT	GTC	644
	Ser	Ser	Ile	Leu	Gly	Arg	Val	Ala	Phe	Phe	Val	Gly	Gly	Tyr	Cys	Val	
			165					170					175				
	TCC	AAG	TAT	GGA	GTG	GAA	GCC	TTT	TCA	GAT	ATT	CTG	AGG	CGT	GAG	ATT	692
	Ser	Lys	Tyr	Gly	Val	Glu	Ala	Phe	Ser	Asp	Ile	Leu	Arg	Arg	Glu	Ile	
25		180					185					190					
	CAA	CAT	TTT	GGG	GTG	AAA	ATC	AGC	ATA	GTT	GAA	CCT	GGC	TAC	TTC	AGA	740
	Gln	His	Phe	Gly	Val	Lys	Ile	Ser	Ile	Val	Glu	Pro	Gly	Tyr	Phe	Arg	
	195					200					205					210	
	ACG	GGA	ATG	ACA	AAC	ATG	ACA	CAG	TCC	TTA	GAG	CGA	ATG	AAG	CAA	AGT	788
30	Thr	Gly	Met	Thr	Asn	Met	Thr	Gln	Ser	Leu	Glu	Arg	Met	Lys	Gln	Ser	
					215					220					225		
	TGG	AAA	GAA	GCC	CCC	AAG	CAT	ATT	AAG	GAG	ACC	TAT	GGA	CAG	CAG	TAT	836
	Trp	Lys	Glu	Ala	Pro	Lys	His	Ile	Lys	Glu	Thr	Tyr	Gly	Gln	Gln	Tyr	
				230					235					240			
35	TTT	GAT	GCC	CTT	TAC	AAT	ATC	ATG	AAG	GAA	GGG	CTG	TTG	AAT	TGT	AGC	884
	Phe	Asp	Ala	Leu	Tyr	Asn	Ile	Met	Lys	Glu	Gly	Leu	Leu	Asn	Cys	Ser	
			245					250					255				
	ACA	AAC	CTG	AAC	CTG	GTC	ACT	GAC	TGC	ATG	GAA	CAT	GCT	CTG	ACA	TCG	932

	Thr Asn Leu Asn Leu Val Thr Asp Cys Met Glu His Ala Leu Thr Ser	
	260 . 265 . 270	
	GTG CAT CCG CGA ACT CGA TAT TCA GCT GGC TGG GAT GCT AAA TTT TTC	980
	Val His Pro Arg Thr Arg Tyr Ser Ala Gly Trp Asp Ala Lys Phe Phe	
5	275 280 285 290	
	TTC ATC CCT CTA TCT TAT TTA CCT ACA TCA CTG GCA GAC TAC ATT TTG	1028
	Phe Ile Pro Leu Ser Tyr Leu Pro Thr Ser Leu Ala Asp Tyr Ile Leu	
	295 300 305	
	ACT AGA TCT TGG CCC AAA CCA GCC CAG GCA GTC TAAAGAAAAC TGGGTTGGT	1080
10	Thr Arg Ser Trp Pro Lys Pro Ala Gln Ala Val	
	310 315	
	GCTTCTTGGA ATGAAGGCAA AAATCTGAAA TTGTTAGTGT CTCAGTAATC CTGATTTAGA	1140
	ACCCAGGCTT TTTGTAACAA TGTGTTTTCT TGCCTAAATT CATTTATCTG GCATCATCAG	1200
	AGTACTAACA TGTTTATATT TCAGATATCC AAAGCTTACC ACTTTAGGTG ATGAATCTTT	1260
15	ACTATTTTAG CCCTTTTTTG ATGAGACTAT TTGTCTAAAG TGAATCATTT GTTCTTGCCT	1320
	TATTAAACAG AGTAGATGGA AAACAATTT	1349
	(2) INFORMATION FOR SEQ ID NO: 39:	
20	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1643	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
25	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Liver	
30	(D) CLONE NAME: HP01347	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
2 =	(B) EXISTENCE POSITION: 25 915	
35	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:	

	AAC	ATCT	GGG (GACA	GCGG	GA A											5:
]		Ser .	Asp	Ser	-	Glu	Pro	Arg	Val	
	CAG	CAG	CTG	GGC	CTC	CTG	GGG	1 тст	СТТ	GGC	САТ	5 660	GCC	CTG	стс	CTG	99
5																Leu	,
J	10			V-)		15	- -,	U) 0	Dou	01)	20	01)				25	
		CTC	CTC	TCC	TTC		CTC	TTG	GCT	GGG		CTG	GTG	GCC	ATC	CTT	147
																Leu	
					30					35					40		
10	GTC	CAA	GTG	TCC	AAG	GTC	CCC	AGC	TCC	CTA	AGT	CAG	GAA	CAA	TCC	GAG	195
	Val	Gln	Val	Ser	Lys	Val	Pro	Ser	Ser	Leu	Ser	Gln	Glu	Gln	Ser	Gļu	
				45					50					55			
	CAA	GAC	GCA	ATC	TAC	CAG	AAC	CTG	ACC	CAG	CTT	AAA	GCT	GCA	GTG	GGT	243
	Gln	Asp	Ala	Ile	Tyr	Gln	Asn	Leu	Thr	Gln	Leu	Lys	Ala	Ala	Val	Gly	
15			60					65					70				
	GAG	CTC	TCA	GAG	AAA	TCC	AAG	CTG	CAG	GAG	ATC	TAC	CAG	GAG	CTG	ACC	291
	Glu	Leu	Ser	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	
		75					80					85					
	CAG.	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	CCA	GAG	AAA	TCC	AAG	CTG	CAG	339
20	Gln	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln	
	90					95					100					105	
	GAG	ATC	TAC	CAG	GAG	CTG	ACC	CGG	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	387
	Glu	Ile	Tyr	Gln	G1u	Leu	Thr	Arg	Leu	Lys	Ala-	-Ala	Val	Gly	Glu	Leu	
					110					115					120		
25				TCC													435
	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	Arg	Leu	
				125					130					135			
				GTG													483
20	Lys	Ala		Val	Gly	Glu	Leu		Glu	Lys	Ser	Lys		Gln	Glu	Ile	
30	m o	040	140	O M O			0.00	145					150				500
				CTG													531
	Tyr		GIU	Leu	Thr	Arg		ras	Ala	Ala	val		Glu	Leu	Pro	Glu	
		155 TCC	A A C	CTC	CAC	CAC	160	TA C	C 4 C	C 4 C	c m c	165	0.40	0.00	440	COT	570
35				CTG Leu													579
	170	261	פעם	neu	GIII	175	116	TYL	9111	GIU	180	THE	GIU	Leu	туя	185	
		GTG	GGT	GAG	TTG		GAG	AAA	TCC	AAG		CAG	GAG	ATC	TAC		627
				Glu													027

126

					190					195					200		
	GAG	CTG	ACC	CAG	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	CCA	GAC	CAG	TCC	675
	Glu	Leu	Thr	Gln	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Asp	Gln	Ser	
				205					210					215			
5	AAG	CAG	CAG	CAA	ATC	TAT	CAA	GAA	CTG	ACC	GAT	TTG	AAG	ACT	GĊA	TTT	723
	Lys	Gln	Gln	Gln	Ile	Tyr	Gln	Glu	Leu	Thr	Asp	Leu	Lys	Thr	Ala	Phe	
			220					225					230				
	GAA	CGC	CTG	TGC	CGC	CAC	TGT	CCC	AAG	GAC	TGG	ACA	TTC	TTC	CAA	GGA	771
	Glu	Arg	Leu	Cys	Arg	His	Cys	Pro	Lys	Asp	Trp	Thr	Phe	Phe	Gln	Gly	
10		235					240					245					
	AAC	TGT	TAC	TTC	ATG	TCT	AAC	TCC	CAG	CGG	AAC	TGG	CAC	GAC	TCC	GTC	819
	Asn	Cys	Tyr	Phe	Met	Ser	Asn	Ser	Gln	Arg	Asn	Trp	His	Asp	Ser	Val	
	250					255					260					265	
	ACC	GCC	TGC	CAG	GAA	GTG	AGG	GCC	CAG	CTC	GTC	GTA	ATC	AAA	ACT	GCT	867
15	Thr	Ala	Cys	Gln	Glu	Val	Arg	Ala	G1n	Leu	Val	Val	Ile	Lys	Thr	Ala	
					270					275					280		
	GAG	GAG	CAG	CTT	CCA	GCG	GTA	CTG	GAA	CAG	TGG	AGA	ACC	CAA	CAA		912
	Glu	Glu	Gln	Leu	Pro	Ala	Val	Leu	Ğlu	Gln	Trp	Arg	Thr	Gln	Gln		
				285					290					295			
20	TAGO	GGGA	AT C	SAAGA	CTGI	G CG	GAAT	TTAG	TGG	CAGI	rggc	TGGA	ACGA	CA A	TCGA	TGT	970
	GAC	TTGA	ACA A	ATTAC	CTGGA	T C	GCAA	AAAG	ccc	GCAG	CCT	GCTI	CAGA	GA C	GAAT	AGTTG	1030
	TTTC	CCTC	CT A	GCCI	CAGC	C TC	CATI	GTGG	TAT	'AGCA	GAA	CTTC	ACCC	AC 1	TGTA	AGCCA	1090
	GCGC	TTCI	TC T	CTCC	CATCO	T TO	GACC	TTCA	CAA	ATGC	CCT	GAGA	CGGI	TC I	CTGI	TCGAT	1150
	TTTI	CATO	cc c	TATG	AACC	T GG	GTCI	TATI	CTG	TCCI	TCT	GATG	CCTC	CA A	GTTT	CCCTG	1210
25	GTGT	'AGAG	CT 1	GTGI	TCTI	G GC	CCAT	CCTI	GGA	GCTI	TAT	AAGI	'GACC	TG A	GTGG	GATGC	1270
	ATTI	'AGGG	GG C	GGGC	TTGG	T AT	GTTG	TATG	LAA	CCAC	TCT	CTGT	TCCI	TT I	GGAG	ATTAG	1330
	ACTA	TTTG	GA I	TCAT	GTGI	'A GC	TGCC	CTGT	ccc	CTGG	GGC	TTTA	TCTC	AT C	CATG	CAAAC	1390
	TACC	ATCI	GC I	CAAC	TTCC	A GC	TACA	cccc	GTG	CACC	CTT	TTGA	.CTGG	GG A	CTTG	CTGGT	1450
	TGAA	GGAG	CT C	ATCI	TGCA	.G GC	TGGA	AGCA	CCA	.GGGA	ATT	AATT	cccc	CA G	TCAA	CCAAT	1510
30	GGCA	TCCA	GA G	AGGG	CATG	G AG	GCTC	CATA	CAA	CCTC	TTC	CACC	CCCA	CA T	CTTT	CTTTG	1570
	TCCT	ATAC	AT G	TCTT	'CCAT	T TG	GCTG	TTTC	TGA	GTTG	TAG	CCTT	TATA	AT A	AAGT	GGTAA	1630
	ATGI	TGTA	AC T	'GC													1643

35 (2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 729
 - (B) TYPE: Nucleic acid

				(0)	STR	ANDE	DNES	S: D	oubl	e							
				(D)	TOP	OLOG	Y: L	inea	r								
		(ii)	SEQU	ENCE	KIN	D: c	DNA	to m	RNA							
5		(vi)	ORIG	INAL	sou	RCE:										
				(A)	ORG.	ANIS	M: <i>H</i>	ото	sapi	ens							
				(B)	CEL	L KI	ND:	Stom	ach	canc	er						
				(D)	CLO	NE N	AME:	HP0	1440								
10		(ix)	SEQU	ENCE	СНА	RACT	ERIS	TICS	:							
				(A)	CHA	RACT	ERIZ.	ATIO	N CO	DE:	CDS						
				(B)	EXI	STEN	CE P	OSIT	ION:	38.	. 63	1					
				(C)	CHA	RACT	ERIZ.	ATIO	N ME	THOD	: E						
15		(:	xi)	SEQU:	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	40:					
	ACT:	rtca(CTC .	ACCG	CCTG	TC C	TTCC	TGAC.	A CC	TCAC	C AT	G TG	T AC	G GG	A AA	A TGT	5
											Me	t Cy	s Th	r Gl	y Ly	s Cys	
												1				5	
20				GTG													10
	Ala	Arg		Val	Gly	Leu	Ser	Leu	Ile	Thr	Leu	Cys	Leu	Val	Cys	Ile	
				10				,	15				:	20			
				GCC													15
	Val	Ala		Ala	Leu	Leu	Leu	Val	Pro	Asn	Gly	Glu	Thr	Ser	Trp	Thr	
25			25					30					35				
				CAT													19
	Asn		Asn	His	Leu	Ser		Gln	Val	Trp	Leu	Met	Gly	Gly	Phe	Ile	
		40					45					50					
20				CTA													24
30		GIY	GLY	Leu	Met		Leu	Cys	Pro	Gly		Ala	Ala	Val	Arg		
	55	000		000	ma.a	60		•••			65					70	
				GGC													29
	GIA	сту	Lys	Gly	_	Cys	GLA	Ala	Gly	•	Cys	Gly	Asn	Arg	•	Arg	
35	A TO C	CTC.	000	mcc.	75	mmo	m00	maa		80					85		0.4
				TCG	30									,			34:
	110 6	neu	vrR	Ser 90	vaı	File	Ser	ser	95	rne	GIÀ	val	Leu	100	VIS	TIG	
	TAC	ፐርር	CTC	TCG	ርጥር	ጥርጥ	GG A	ርርቱ		CTC	CGA	ልልጥ	GG A		AGA	ጥርር	39:
		-00	- 10	- OG	- 1 G	101	GGV	GO 1	GGG	-10	CGM	uul	GGM		VAW	190	27.

128

	Tyr	Cys	Leu	Ser	Val	Ser	Gly	Ala	Gly	Leu	Arg	Asn	Gly	Pro	Arg	Cys	
			105					110					115				
	TTA	ATG	AAC	GGC	GAG	TGG	GGC	TAC	CAC	TTC	GAA	GAC	ACC	GCG	GGA	GCT	439
	Leu	Met	Asn	Gly	Glu	Trp	Gly	Tyr	His	Phe	Glu	Asp	Thr	Ala	Gly	Ala	
5		120					125					130					
	TAC	TTG	CTC	AAC	CGC	ACT	CTA	TGG	GAT	CGG	TGC	GAG	GCG	CCC	CCT	CGC	487
	Tyr	Leu	Leu	Asn	Arg	Thr	Leu	Trp	Asp	Arg	Cys	Glu	Ala	Pro	Pro	Arg	
	135					140					145					150	
	GTG	GTC	CCC	TGG	AAŢ	GTG	ACG	CTC	TTC	TCG	CTG	CTG	GTG	GCC	GCC	TCC	535
10	Val	Val	Pro	Trp	Asn	Val	Thr	Leu	Phe	Ser	Leu	Leu	Val	Ala	Ala	Ser	
					155					160					165		
	TGC	CTG	GAG	ATA	GTA	CTG	TGT	GGG	ATC	CAG	CTG	GTG	AAC	GCG	ACC	ATT	583
	Cys	Leu	Glu	Ile	Val	Leu	Cys	Gly	Ile	Gln	Leu	Val	Asn	Ala	Thr	Ile	
				170					175					180			
15	GGT	GTC	TTC	TGC	GGC	GAT	TGC	AGG	AAA	AAA	CAG	GAC	ACC	CCT	CAC	TG	630
	Gly	Val	Phe	Cys	Gly	Asp	Cys	Arg	Lys	Lys	Gln	Asp	Thr	Pro	His		
			185					190					195				
	AGG(CTCCA	ACT (GACC	CCG	G TI	CACAC	CTG	TCC	CTTCC	TGG	ACG	CTAC	CT	GCTC	CGCTCA	690
	CTC	CTT	GCT (CGCTA	AGAA:	AA Aî	CTG	CTTTC	CGC	CTCTC	TT						729
20																	
						•											
	(2)		ORMAI			•											
		(:	i) SI	•					CS:								
				• •		TH:											
25	٠.					E: Nu											
						INDEI				•							
						LOGY											
		()	ii) S	FQUI	ENCE	KINI): CI)NA t	o mb	KNA							
30		(3	/i) (ופדפו	ΓΝΙΔΙ	SOITE	CF.										
, ,		(,	, 1) (NISM		3mo 4	ani.	n 0							
						KIN			•								
						IE NA				ance							
				(-)	-201	4127		01									
35		t)	lx) S	EQUE	ENCE	CHAR	ACTE	ERIST	CICS:								
						LACTE					DS	-					
						TENC)					

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

	GAG	CCGC	AGG	TCTG	GGCT	GC A	GTAG	GTCC	C GG	CAA	CCGC	CA G	GCI	rcgc	GGC	GGG	CGC	TGGG		60
	CGC	GGGA'	TCC	GACT	CTAG	TC G	TA A	TG G	AG G	CG	GGC	GGC	тТ	T C	TG	GAC	TCG	CTC	1	113
5							М	et G	lu A	la	Gly	Gly	Ph	ie L	eu .	Asp	Ser	Leu		
								1				5						10		
	ATT	TAC	GGA	GCA	TGC	GTG	GTC	TTC	ACC	CT	T GG	C A	TG.	TTC	TC	C GC	C G	GC	3	L61
	Ile	Tyr	Gly	Ala	Ċys	Val	Val	Phe	Thr	Le	u Gl	у М	et	Phe	Se	r Al	a G	ly		
					15					2	0					2	.5			
10	CTC	TCG	GAC	CTC	AGG	CAC	ATG	CGA	ATG	AC	C CG	G A	GT	GTG	GA	C AA	C G	TC	2	209
	Leu	Ser	Asp	Leu	Arg	His	Met	Arg	Met	Th	r Ar	g S	er	Val	As	p As	n V	al		
				30					35						4	0				
	CAG	TTC	CTG	CCC	TTT	CTC	ACC	ACG	GAA	GT	C AA	C A	AC	CTG	GG	C TG	G C	TG	2	257
	Gln	Phe	Leu	Pro	Phe	Leu	Thr	Thr	Glu	۷a	l As	n A	sn	Leu	G1	y Tr	p L	eu		
15			45					50						55						
	AGT	TAT	GGG	GCT	TTG	AAG	GGA	GAC	GGG	AT	с ст	C A	TC	GTC	GT	C AA	C A	CA	3	805
	Ser	Tyr	Gly	Ala	Leu	Lys	Gly	Asp	Gly	11	e Le	u I	le	Val	Va:	l As	n T	hr		
		60					65						70							
	GTG	GGT	GCT	GCG	CTT	CAG	ACC	CTG	TAT	AT	C TT	G G	CA	TAT	CTO	G CA	т т.	AC	3	53
20	Val	Gly	Ala	Ala	Leu	Gln	Thr	Leu	Tyr	Il	e Le	u A	la	Tyr	Let	ı Hi	s T	yr		
	75					80					8	5						90		
	TGC	CCT	CGG	AAG	CGT	GTT	GTG	CTC	CTA	CA	G AC	T G	CA	ACC	CTO	CT	A G	GG	4	01
	Cys	Pro	Arg	Lys	Arg	Val	Val	Leu	Leu	Gli	n Th	r A	la	Thr	Let	ı Le	u G	ly		
					95					10	ס					10	5			
25	GTC	CTT	CTC	CTG	GGT	TAT	GGC	TAC	TTT	TG	G CT	C C	TG	GTA	CCC	C AA	C C	CT	4	49
	Val	Leu	Leu	Leu	Gly	Tyr	Gly	Tyr	Phe	Tr	p Le	u L	eu	Val	Pro	As	n P	ro		
				110					115						120)				
	GAG	GCC	CGG	CTT	CAG	CAG	TTG	GGC	CTC	TTC	C TG	C A	GT	GTC	TTC	CAC	C A	rc	4	97
	Glu	Ala	Arg	Leu	Gln	Gln	Leu	Gly	Leu	Phe	∋ Су	s S	er	Val	Phe	e Th	r I	le		
30			125					130						135						
	AGC	ATG	TAC	CTC	TCA	CCA	CTĢ	GCT	GAC	TTC	G GC	T A	AG	GTG	ATT	CA	A A	CT	5	45
	Ser	Met	Tyr	Leu	Ser	Pro	Leu	Ala	Asp	Let	ı Al	a L	ys '	Val	Ile	e G1	n Tl	nr		
		140					145					1.	50							
	AAA	TCA	ACC	CAA	TGT	CTC	TCC	TAC	CCA	CTO	CAC	C A	TT	GCT	ACC	CT	T C	rc	5	93
35	Lys	Ser	Thr	Gln	Cys	Leu	Ser	Tyr	Pro	Let	ı Th	r I	le .	Ala	Thi	Le	u Le	eu		
	155					160					16	5					1	70		
	ACC	TCT	GCC	TCC	TGG	TGC	CTC	TAT	GGG	TT	r cg	A C	TC .	AGA	GAT	CC	C T	ΑT	6	41
	Thr	Ser	Ala	Ser	Trp	Cys	Leu	Tyr	G1y	Phe	Ar	g Le	eu .	Arg	Ast	Pr	o Ty	r		

	175 180 185	
	ATC ATG GTG TCC AAC TTT CCA GGA ATC GTC ACC AGC TTT ATC CGC TTC	689
	Ile Met Val Ser Asn Phe Pro Gly Ile Val Thr Ser Phe Ile Arg Phe	
	190 195 200	
5	TGG CTT TTC TGG AAG TAC CCC CAG GAG CAA GAC AGG AAC TAC TGG CTC	737
	Trp Leu Phe Trp Lys Tyr Pro Gln Glu Gln Asp Arg Asn Tyr Trp Leu	
	205 210 215	
	CTG CAA ACC TGAGGCTGCT CATCTGACCA CTGGGCCACCT TAGTGCCAAC CTGA	790
	Leu Gln Thr	
10	220	
	ACCAAAGAGA CCTCCTTGTT TCAGCTGGGC CTGCTGTCCA GCTTCCCAGG TGCAGTGGGT	850
	TGTGGGAACA AGAGATGACT TTGAGGATAA AAGGACCAAA GAAAAAGCTT TACTTAGATG	910
	ATTGATTGGG GCCTAGGAGA TGAAATCACT TTTTATTTTT TAGAGATTTT TTTTTTTAAT	970
	TTTGGAGGTT GGGGTGCAAT CTTTAGAATA TGCCTTAAAA GGCCGGGCGC GGTGGCTCAC	1030
15	GCCTGTAATC CCAGCACTTT GGGAGGCCAA GGTGGGCGGA TCGCCTGAGG TCAGGAGTTC	1090
	AAGACCAACC TGACTAACAT GGTGAAACCC CATCTCTACT AAAAATACAA AATTAGCCAG	1150
	GCATGATGGC ACATGCCTGT AATCCCAGAT ACTTGGGAGG CTGAGGCAGG AGAATTGCTT	1210
	GAACCCAGGA GGTGGAGGTT GCAGTGAGCT GAGATCGTGC CATTGTGATA TGAATATGCC	1270
• •	TTATATGCTG ATATGAATAT GCCTTAAAAT AAAGTGTTCC CCACCCCTGC CC	1322
20		
	(C) TURONYARTON ROD ORG. TO ME	
	(2) INFORMATION FOR SEQ ID NO: 42:	
	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 3045	
25	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
30	(vi) ORIGINAL SOURCE:	
•	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10230	
	(b) Cloth Mail: III 10230	
35	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 191 946	
	(C) CHARACTERIZATION METHOD: E	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

	GTT'	rcgc	CTC .	AGAA	.GGCT	GC C	TCGC	TGGI	DO. 07	TAA	CGGT	GGC	GCCA	.CGT	CCGC	CCGTC	т 60
	CCG	CCTT	CTG	CATC	GCGG	CT I	CGGC	GGCI	T CC	CACCI	CAGAC	ACC	TAAC	AGT	CGCG	GAGCC	G 120
5	GCC	GCGT	CGT	GAGG	GGGT	CG G	CACG	GGGA	G TO	GGGC	GGTC	TTG	TGCA	TCT	TGGC	TACCT	G 180
	TGG	STCG	AAG .	ATG	TCG	GAC	ATC	GGA	GAC	TGG	TTC	AGG	AGC	ATC	CCG	GCG	229
			1	Met	Ser	Asp	Ile	Gly	Asp	Trp	Phe	Arg	Ser	Ile	Pro	Ala	
				1				5					10				
	ATC	ACG	CGC	TAT	TGG	TTC	GCC	GCC	ACC	GTC	GCC	GTG	CCC	TTG	GTC	GGC	277
10	Ile	Thr	Arg	Tyr	Trp	Phe	Ala	Ala	Thr	Val	. Ala	Val	Pro	Leu	Val	Gly	
		15					20					25					
	AAA	CTC	GGC	CTC	ATC	AGC	CCG	GCC	TAC	CTC	TTC	CTC	TGG	CCC	GAA	GCC	325
	Lys	Leu	Gly	Leu	Ile	Ser	Pro	Ala	Tyr	Leu	Phe	Leu	Trp	Pro	Glu	Ala	
	30					35					40					45	
15							ATT										373
	Phe	Leu	Tyr	Arg		Gln	Ile	Trp	Arg	Pro	Ile	Thr	Ala	Thr	Phe	Tyr	
					50					55					60		
							ACT										421
•	Phe	Pro	Val			Gly	Thr	Gly			Tyr	Leu	Val		Leu	Tyr	
20	mme	mm 4		65					70					75			
							ACG										469
	Pne	Leu		GIn	Tyr	Ser	Thr			Glu	Thr	Gly		Phe	Asp	Gly	
	400	204	80	0.40	m 4 m	mm 4		85					90				52.7
2 E							TTC										517
25	Arg		ALE	Asp	Tyr	Leu	Phe	Met	Leu	Leu	Phe		_	IIe	Cys	IIe	
	CTC	95	4.Cm		mm A	004	100	O 4 M		0.40	mmo	105	•	4 mm	000	omo	5.5
							ATG										565
	110	116	int	GIY	Leu		Met	Asp	met	GIN		Leu	met	ire	Pro		
30		ΔTG	ጥ ር ል	GΨA	Շ դրդու	115	GTC	TCC	CCC	CAC	120	4 A C	A C A	CAC	<u>ለ ጥ</u> ር	125	612
50							Val										613
	110	1100	Jer	407	130	Tyl	V41	тър	, via	.135		VPII	ALE	wsh	140	116	
	СТА	ТСΔ	ጥጥጥ	TGG		GG A	ACA	CGA	ጥጥጥ			ጥርር	ጥለጥ	ጥጥለ		TCC	661
							Thr										001
35		001	1	145		01)		··- 5	150		nia	Oys	Tyr	155	110	11.5	
	GTT	ATC	СТТ			AAC	TAT	ATC			GGC	ፐርር	GΤA		ДАТ	GAG	709
							Tyr										. 55
	-		160	,			-,-	165)	/		170				
													•				

PCT/JP98/02445

	CTT	ATT	GGA	AAT	CTG	GTT	GGA	CAT	CTT	TAT	TTT	TTC	CTA	ATG	TTC	AGA	757
	Leu	Ile	Gly	Asn	Leu	Val	Gly	His	Leu	Tyr	Phe	Phe	Leu	Met	Phe	Arg	
		175					180					185					
	TAC	CCA	ATG	GAC	TTG	GGA	GGA	AGA	AAT	TTT	CTA	TCC	ACA	CCT	CAG	TTT	805
5	Tyr	Pro	Met	Asp	Leu	Gly	Gly	Arg	Asn	Phe	Leu	Ser	Thr	Pro	Gln	Phe	
	190					195					200					205	
	TTG	TAC	CGC	TGG	CTG	CCC	AGT	AGG	AGA	GGA	GGA	GTA	TCA	GGA	TTT	GGT	853
	Leu	Tyr	Arg	Trp	Leu	Pro	Ser	Arg	Arg	Gly	Gly	Val	Ser	Gly	Phe	Gly	
					210					215					220		
10	GTG	CCC	CCT	GCT	AGC	ATG	AGG	CGA	GCT	GCT	GAT	CAG	AAT	GGC	GGA	GGC	901
٠	Val	Pro	Pro	Ala	Ser	Met	Arg	Arg	Ala	Ala	Asp	Gln	Asn	Gly	Gly	Gly	
				225					230					235			
	GGG	AGA	CAC	AAC	TGG	GGC	CAG	GGC	TTT	CGA	CTT	GGA	GAC	CAG	TGA	AGGG	950
	Gly	Arg	His	Asn	Trp	Gly	Gln	Gly	Phe	Arg	Leu	Gly	Asp	Gln			
15			240					245					250				
	GCG	CCT	CGG (GCAGC	CCGC	rc c	CTC	AAGCC	ACA	TTTC	CTC	CCAC	TGC	rgg (TGC	CTTAA	1010
																CAGTAC	1070
																SATTCT	1130
	CAT	CAAC	GTC (CTTAC	CTGC	rg to	SAAGA	AACAA	ATA	CCAA	ACTG	TGCA	TAAL	rgc A	AAAA	CTGACT	1190
20	ACA:	TTTT:	TG (GTGTC	CTTCI	C T	CTC	CCTI	TCC	GTCI	GAA	TAAT	rggg1	TTT 1	CAGCO	GGTCC	1250
	TAG	CTG	CTG (GCATI	GAGC	CT GO	GGC1	rgggi	CAC	CAAA	CCC	TTCC	CAAA	AAG (ACCC	TTATC	1310
																CAGAAG	1370
																GCCAA	1430
																TAGCA	1490
25	ATAC	GGGG	GAG A	AAGAC	CAAGO	CA GO	CGGAI	'GAAG	CGI	TTTC	TCA	GCTI	TTGG	SAA 7	TGCI	TCGAC	1550
	CTGA	ACATO	CCG 1	TGTA	ACCG	T T	GCCA	ACTTO	TTC	AGAT	TTA	TTTA	TAAA	AAA A	GTAC	CACTG	1610
	AGT	CAGTO	GAG (GCCA	CAGA	T TO	GTAT	TAAT	GAG	ATAC	GAG	GGTI	GTTG	CT G	GGTG	TTTGT	1670
																AAATT	1730
																GCTGG	1790
30														•		TGCTC	1850
																TCATT	1910
																CCCCG	1970
																AGATC	2030
2 -																ATGGC	2090
35			_													CTGTG	2150
																AGAGC	2210
																TTATT	2270
	7.7.4.4	LACC	יוייוי. 🖊	. ሳተረጉ ጥረት	. ^ ^ ^ ^	· · · · · · · · · · · · · · · · · · ·	- ላ ጣጥሶ	· ጥጥ A 🔿	$\alpha \wedge \alpha$	~ A ~ T	· A 170 170	CAOR	$\alpha \alpha \alpha \pi$	·~ ·	· * ~ * ~	· ••• •• • • • • • • • • • • • • • • •	つつつ∧

				133			
	GGCAACTAAA	AAGGCTTCAA ACC	STTTTGAT	CAGTTTCTTT	TCAGGAAACA	TTGTGCTCTA	2390
	ACAGTATGAC	TATTCTTTCC CCC	CACTCTTA	AACAGTGTGA	TGTGTGTTAT	CCTAGGAAAT	2450
	GAGAGTTGGC	AAACAACTTC TCA	ATTTTGAA	TAGAGTTTGT	GTGTACCTCT	CCATATTTAA	2510
	TTTATATGAT	AAAATAGGTG GGG	SAGAGTCT	GAACCTTAAC	TGTCATGTTT	TGTTGTTCAT	2570
5	CTGTGGCCAC	AATAAAGTTT ACT	TTGTAAAA	TTTTAGAGGC	CATTACTCCA	ATTATGTTGC	2630
	ACGTACACTC	ATTGTACAGG CG	GGAGACT	CATTGTATGT	ATAAGAATAT	TCTGACAGTG	2690
	AGTGACCCGG	AGTCTCTGGT GTA	ACCCTCTT	ACCAGTCAGC	TGCCTGCGAG	CAGTCATTTT	2750
	TTCCTAAAGG	TTTACAAGTA TT	TAGAACTC	TTCAGTTCAG	GGCAAAATGT	TCATGAAGTT	2810
	ATTCCTCTTA	AACATGGTTA GGA	AGCTGAT	GACGTTATTG	ATTTTGTCTG	GATTATGTTT	2870
LO	CTGGAATAAT	TTTACCAAAA CAA	GCTATTT	GAGTTTTGAC	TTGACAAGGC	AAAACATGAC	2930
	AGTGGATTCT	CTTTACAAAT TGA	AAAAAA	AATCCTTATT	TTGTATAAAG	GACTTCCCTT	2990
	TTTGTAAACT	AATCCTTTTT AT	rggtaaaa	ATTGTAAATT	AAAATGTGCA	ACTTG	3045
15	(2) INFORM	TION FOR SEQ	ID NO: 43	3:			
	(i)	EQUENCE CHARAC	CTERISTIC	CS:			
		(A) LENGTH: 6	553				
		(B) TYPE: Nuc	cleic aci	.d			
		(C) STRANDED	NESS: Dou	ıble			
20		(D) TOPOLOGY:	Linear				
	(ii)	SEQUENCE KIND:	cDNA to	mRNA			
	(vi)	ORIGINAL SOURC					
		(A) ORGANISM:		-			
25		(B) CELL KINI		moid carcin	noma		
		(C) CELL LINE					
		(D) CLONE NAM	4E: HP103	189			
	/ 2 \	CECHENCE CHAP					
30	(1X)	SEQUENCE CHARA					
U		(A) CHARACTER	CIZATION	CODE: CDS			

(B) EXISTENCE POSITION: 63.. 383

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

35

ATGACCTTCA CCGGGAGGCT GAGGTCGGAG TCCCGATTTT CTCCTGCTGC TGTGGCCCGG 60

AC ATG GCG ACT CCC GGC CCT GTG ATT CCG GAG GTC CCC TTT GAA CCA 107

Met Ala Thr Pro Gly Pro Val Ile Pro Glu Val Pro Phe Glu Pro

134

		1				5					10					15		
	TCG	AAG	CCT	CCA	GTC	ATT	GAG	GGG	CTG	AGC	CCC	ACT	GTT	TAC	AGG	AAT	•	155
	Ser	Lys	Pro	Pro	Val	Ile	Glu	Gly	Leu	Ser	Pro	Thr	Val	Tyr	Arg	Asn		
					20					25	•				30			
5	CCA	GAG	AGT	TTC	AAG	GAA	AAG	TTC	GTT	CGC	AAG	ACC	CGC	GAG	AAC	CCG	:	203
	Pro	Glu	Ser	Phe	Lys	Glu	Lys	Phe	Val	Arg	Lys	Thr	Arg	Glu	Asn	Pro		
				35					40					45				
	GTG	GTA	CCC	ATA	GGT	TGC	CTG	GCC	ACG	GCG	GCC	GCC	CTC	ACC	TAC	GGC	2	251
	Val	Val	Pro	Ile	Gly	Cys	Leu	Ala	Thr	Ala	Ala	Ala	Leu	Thr	Tyr	Gly		
10			50					55					60					
	CTC	TAC	TCC	TTC	CAC	CGG	GGC	AAC	AGC	CAG	CGC	TCT	CAG	CTC	ATG	ATG	:	299
	Leu	Tyr	Ser	Phe	His	Arg	Gly	Asn	Ser	Gln	Arg	Ser	Gln	Leu	Met	Met		
		65					70					75						
	CGC	ACC	CGG	ATC	GCC	GCC	CAG	GGT	TTC	ACG	GTC	GCA	GCC	ATC	TTG	CTG	:	347
15	Arg	Thr	Arg	Ile	Ala	Ala	Gln	G1y	Phe	Thr	Va1	Ala	Ala	Ile	Leu	Leu		
	80					85					90					95		
	GGT	CTG	GCT	GTC	ACT	GCT	ATG	AAG	TCT	CGA	CCC	TAAC	GCCC	AGG (GTCT	GCCTT	: 4	400
	Gly	Leu	Ala	Val	Thr	Ala	Met	Lys	Ser	Arg	Pro							
					100					105								
20	GAAA	AGCT	CCG	CAGA	AATG	AT T	CCAA	AACC	C AGO	GGAG	CAAC	CAC	rggc	CCT	ACCG'	rgggac	: 4	460
	TTAC	CTCC	CTC (CTCT	CCTT'	rg ac	GAGG	CCCA!	r GT(GTCG	CTGG	GGAC	GAAG	GTG A	ACCC'	rttgtg		520
																CATACI		580
	TCTA	\TTT(GTG (CCAC	ATCT(CC CC	CTCC	ACTC	c cc:	rgct'	TAAT	AAA(CTCTA	AAA .	AATC	CACTTG		540
	TAT	TAA'	TTC A	AGT													(553
25																		
						Δ.												
	(2)			TION		•												
		(:	1) S	EQUE				RIST.	ICS:									
20						STH:												
30							ucle:											
									ouble	е								
		,					Y: L:											
		(:	11) :	SEQU	ENCE	KINI	D: CI	DNA 1	co mi	KNA								
35		/-	v-11 /	ORIG	TNAT	SULL	- ब											
-		(• -)					omo	sapi	ene								
									-	cance	er							
				/	. ~													

(D) CLONE NAME: HP10408

135

(ix) SEQUENCE CHARACTERISTICS:

	(A)	CHARACTERIZA	ATION CODE:	CDS		
	(B)	EXISTENCE PO	OSITION: 75	311		
	(C)	CHARACTERIZA	ATION METHOI	D: E		
5						
	(xi) SEQU	ENCE DESCRIP	TION: SEQ II	NO: 44:		
	GTAGAAACAG GCCT	GTTAAG GAGAG	GCCAC CGGGAC	CTTCA GTGTCTC	CTC CATCCCAGGA	60
	GCGCAGTGGC CACT	ATG GGG TCT	GGG CTG CCC	CTT GTC CTC	CTC TTG ACC	110
10		Met Gly Ser	Gly Leu Pro	Leu Val Leu	Leu Leu Thr	
		1	5		10	
	CTC CTT GGC AGC	TCA CAT GGA	ACA GGG CCG	GGT ATG ACT	TTG CAA CTG	158
	Leu Leu Gly Ser	Ser His Gly	Thr Gly Pro	Gly Met Thr	Leu Gln Leu	
	15		20	25	٠	
15	AAG CTG AAG GAG	TCT TTT CTG	ACA AAT TCC	TCC TAT GAG	TCC AGC TTC	206
	Lys Leu Lys Glu	Ser Phe Leu	Thr Asn Ser	Ser Tyr Glu	Ser Ser Phe	
	30	35		40		
	CTG GAA TTG CTT	GAA AAG CTC	TGC CTC CTC	CTC CAT CTC	CCT TCA GGG	254
	Leu Glu Leu Leu	Glu Lys Leu	Cys Leu Leu	Leu His Leu	Pro Ser Gly	
20	45	50		55	60	
	ACC AGC GTC ACC					302
	Thr Ser Val Thr	Leu His His	Ala Arg Ser	Gln His His	Val Val Cys	
		65	· 70		75	
	AAC ACA TGACAGC	CAT TGAAGCCTG	ST GTCCTTCTT	G GCCCGGGCTT	TTGGGCCGGG GA	360
25	Asn Thr					
	TGCAGGAGGC AGGC		CTTTC AGCAGG	CCCC CACCCTC	CTG AGTGGCAATA	420
	AATAAAATTC GGTA	TGCTG				439
2.0						
30		· ·				
	(2) INFORMATION	•				
		NCE CHARACTER				
		LENGTH: 1131				
2 E		TYPE: Nuclei				
35		STRANDEDNESS				
		TOPOLOGY: Li				
	(11) SEQUI	ENCE KIND: cl	NA TO MKNA			

(vi) ORIGINAL SOURCE:

				(A)	ORG	ANISI	M: H	ото	sapi	ens							
				(B)	CEL	L KII	ND:	Stom	ach (canc	er						
				(D)	CLO	NE NA	AME:	HP1	0412								
5																	
		(:	ix)	SEQUI	ENCE	CHAI	RACT	ERIS'	rics	:							
				(A)	CHAI	RACT	ERIZA	ATIO	N CO	DE: (CDS						
				(B)	EXI	STEN	CE PO	OSIT:	ION:	56.	. 10	00					
				(C)	CHAI	RACT	ERIZA	ATIO	ME'	THOD	: E						
10																	
		(:	xi) :	SEQUI	ENCE	DES	CRIP'	rion	: SE	QID	NO:	45:					
	CTA?	rgag <i>i</i>	ATC (CCGG	CCTC	AG G	GTGG	ACGC	A GT	GGTT(CTGC	ACT	GAGG	CCC '	TCGT	C ATG	58
																Met	
15																1	
															GGC		106
	Val	Ala	Pro		Trp	Tyr	Leu	Val		Ala	Ala	Leu	Leu		Gly	Phe	
				5					10					15			
•															GGC		154
20	Ile	Leu		Leu	Thr	Arg	Ser	_	Gly	Arg	Ala	Ala		Ala	Gly	GIn	
			20					25					30			240	0.00
															GCC		202
	GIU		Leu	HIS	Asn	GIU		Leu	ATB	GTÀ	Ala	_	Arg	vai	Ala	GIN	
25	CCT	35.	ccc	CTC	CAC	CCT	40	CAC	ccc	A C A	CCT	45	ccc	ACC	CCT	CGG	250
LJ															Pro		250
	50	Oly	110	Deu	GIU	55	GIU	Giu	110	n. P	60	Gly	Gly	nr g	110	65	
		CGG	AGG	GAC	CTG		AGC	CGC	СТА	CAG		CAG	CGT	CGA	GCC		298
															Ala		
30	J	J	J		70	,				75				0	80		
	CGG	GTG	GCC	TGG	GCA	GAA	GCA	GAT	GAG	AAC	GAG	GAG	GAA	GCT	GTC	ATC	346
															Val		
				85				·	90					95			
	CTA	GCC	CAG	GAG	GAG	GAA	GGT	GTC	GAG	AAG	CCA	GCG	GAA	ACT	CAC	CTG	394
35	Leu	Ala	Gln	Glu	Glu	Glu	Gly	Val	Glu	Lys	Pro	Ala	Glu	Thr	His	Leu	
		-	100					105		<u>.</u>			110	-			
	TCG	GGG	AAA	ATT	GGA	GCT	AAG	AAA	CTG	CGG	AAG	CTG	GAG	GAG	AAA	CAA	442
	Ser	Glv	Lys	Ile	Glv	Ala	Lvs	Lvs	Leu	Arg	Lvs	Leu	Glu	Glu	Lvs	Gln	

		115					120					125					
	GCG	CGA	AAG	GCC	CAG	CGT	GAG	GCA	GAG	GAG	GCT	GAA	CGT	GAG	GAG	CGG	490
	Ala	Arg	Lys	Ala	Gln	Arg	Glu	Ala	Glu	Glu	Ala	Glu	Arg	Glu	Glu	Arg	
	130					135					140					145	
5	AAA	CGA	CTC	GAG	TCC	CAG	CGC	GAA	GCT	GAG	TGG	AAG	AAG	GAG	GAG	GAG	538
	Lys	Arg	Leu	Glu	Ser	Gln	Arg	Glu	Ala	Glu	Trp	Lys	Lys	Glu	Glu	Glu	
					150					155					160		
	CGG	CTT	CGC	CTG	GAG	GAG	GAG	CAG	AAG	GAG	GAG	GAG	GAG	AGG	AAG	GCC	586
	Arg	Leu	Arg	Leu	Glu	Glu	Glu	Gln	Lys	Glu	Glu	Glu	Glu	Arg	Lys	Ala	
10				165					170					175			
	CGC	GAG	GAG	CAG	GCC	CAG	CGG	GAG	CAT	GAG	GAG	TAC	CTG	AAA	CTG	AAG	634
	Arg	Glu	Glu	Gln	Ala	Gln	Arg	Glu	His	Glu	Glu	Tyr	Leu	Lys	Leu	Lys	
			180					185					190				
	GAG	GCC	TTT	GTG	GTG	GAG	GAG	GAA	GGC	GTA	GGA	GAG	ACC	ATG	ACT	GAG	682
15	Glu	Ala	Phe	Val	Val	Glu	Glu	Glu	Gly	Val	Gly	Glu	Thr	Met	Thr	Glu	
		195					200					205					
	GAA	CAG	TCC	CAG	AGC	TTC	CTG	ACA	GAG	TTC	ATC	AAC	TAC	ATC	AAG	CAG	730
	Glu	Gln	Ser	Gln	Ser	Phe	Leu	Thr	Glu	Phe	Ile	Asn	Tyr	Ile	Lys	Gln	
	210					215					220					225	
20	TCC	AAG	GTT	GTG	CTC	TTG	GAA	GAC	CTG	GCT	TCC	CAG	GTG	GGC	CTA	CGC	778
	Ser	Lys	Val	Val	Leu	Leu	Glu	Asp	Leu	Ala	Ser	Gln	Val	Gly	Leu	Arg	
					230					235					240		
	ACT	CAG	GAC	ACC	ATA	AAT	CGC	ATC	CAG	GAC	CTG	CTG	GCT	GAG	GGG	ACT	826
	Thr	Gln	Asp	Thr	Ile	Asn	Arg	Ile	Gln	Asp	Leu	Leu	Ala	Glu	Gly	Thr	
25				245					250					255			
	ATA	ACA	GGT	GTG	ATT	GAC	GAC	CGG	GGC	AAG	TTC	ATC	TAC	ATA	ACC	CCA	874
	Ile	Thr	Gly	Val	Ile	Asp	Asp	Arg	Gly	Lys	Phe	Ile	Tyr	Ile	Thr	Pro	
			260					265					270				
	GAG	GAA	CTG	GCC	GCC	GTG	GCC.	AAC	TTC	ATC	CGA	CAG	CGG	GGC	CGG	GTG	922
30	G1u	Glu	Leu	Ala	Ala	Val	Ala	Asn	Phe	Ile	Arg	Gln	Arg	Gly	Arg	Val	
		275					280					285					•
	TCC	ATC	GCC	GAG	CTT	GCC	CAA	GCC-	AGC	AAC	TCC	CTC	ATC	GCC	TGG	GGC	970
	Ser	Ile	Ala	Glu	Leu	Ala	Gln	Ala	Ser	Asn	Ser	Leu	Ile	Ala	Trp	Gly	
	290					295					300					305	
35	CGG	GAG	TCC	CCT	GCC	CAA	GCC	CCA	GCC	TGAC	CCCA	GT C	CTTC	CCTC	T TO	G	1020
	Arg	Glu	Ser	Pro	Ala	Gln	Ala	Pro	Ala								
					310												
	ACTO	AGAG	TT G	GTGT	'GGCC	T AC	CTGG	CTAT	ACA	TCTT	CAT	CCCI	'cccc	AC C	ATC	TGGGG	1080

138

1131

303

AAGTGATGGT GTGGCCAGGC AGTTATAGAT TAAAGGCCTG TGAGTACTGC T

	(2) INFORMATION FOR SEQ ID NO: 46:	
5	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1875	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
10	(ii) SEQUENCE KIND: cDNA to mRNA	
	•	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
15	(B) CELL KIND: Stomach cancer	
13	(D) CLONE NAME: HP10413	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 79 666	
20	(C) CHARACTERIZATION METHOD: E	
	·	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:	
	CTCGCTCGCT CAGAGGGAGG AGAAAGTGGC GAGTTCCGGA TCCCTGCCTA GCGCGGCCCA	60
25	ACCTITACTC CAGAGATC ATG GCT GCC GAG GAT GTG GTG GCG ACT GGC GCC	60 111
	Met Ala Ala Glu Asp Val Val Ala Thr Gly Ala	111
	1 5 10	
	GAC CCA AGC GAT CTG GAG AGC GGC GGG CTG CTG CAT GAG ATT TTC ACG	159
	Asp Pro Ser Asp Leu Glu Ser Gly Gly Leu Leu His Glu Ile Phe Thr	
30	15 20 25	
	TCG CCG CTC AAC CTG CTG CTT GGC CTC TGC ATC TTC CTG CTC TAC	207
	Ser Pro Leu Asn Leu Leu Leu Gly Leu Cys Ile Phe Leu Leu Tyr	
	30 35 40	
	AAG ATC GTG CGC GGG GAC CAG CCG GCG GCC AGC GGC GAC AGC GAC	255
35	Lys Ile Val Arg Gly Asp Gln Pro Ala Ala Ser Gly Asp Ser Asp Asp	

50

GAC GAG CCG CCC CCT CTG CCC CGC CTC AAG CGG CGC GAC TTC ACC CCC

Asp Glu Pro Pro Pro Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro

55

	60					65					70					75	
	GCC	GAG	CTG	CGG	CGC	TTC	GAC	GGC	GTC	CAG	GAC	CCG	CGC	ATA	CTC	ATG	351
	Ala	Glu	Leu	Arg	Arg	Phe	Asp	Gly	Val	Gln	Asp	Pro	Arg	Ile	Leu	Met	
					80					85					90		
5	GCC	ATC	AAC	GGC	AAG	GTG	TTC	GAT	GTG	ACC	AAA	GGC	CGC	AAA	TTC	TAC	399
	Ala	Ile	Asn	Gly	Lys	Val	Phe	Asp	Val	Thr	Lys	Gly	Arg	Lys	Phe	Tyr	
				95					100		•			105			
	GGG	ccc	GAG	GGG	CCG	TAT	GGG	GTC	TTT	GCT	GGA	AGA	GAT	GCA	TCC	AGG	447
	Gly	Pro	Glu	Gly	Pro	Tyr	Gly	Val	Phe	Ala	Gly	Arg	Asp	Ala	Ser	Arg	
10			110					115					120				
	GGC	CTT	GCC	ACA	TTT	TGC	CTG	GAT	AAG	GAA	GCA	CTG	AAG	GAT	GAG	TAC	495
	Gly	Leu	Ala	Thr	Phe	Cys	Leu	Asp	Lys	Glu	Ala	Leu	Lys	Asp	Glu	Tyr	
		125					130					135					
	GAT	GAC	CTT	TCT	GAC	CTC	ACT	GCT	GCC	CAG	CAG	GAG	ACT	CTG	AGT	GAC	543
15	Asp	Asp	Leu	Ser	Asp	Leu	Thr	Ala	Ala	Gln	Gln	Glu	Thr	Leu	Ser	Asp	
	140					145					150					155	
	TGG	GAG	TCT	CAG	TTC	ACT	TTC	AAG	TAT	CAT	CAC	GTG	GGC	AAA	CTG	CTG	591
	Trp	Glu	Ser	Gln	Phe	Thr	Phe	Lys	Tyr	His	His	Val	Gly	Lys	Leu	Leu	
					160					165					170		
20	AAG	GAG	GGG	GAG	GAG	CCC	ACT	GTG	TAC	TCA	GAT	GAG	GAA	GAA	CCA	AAA	639
	Lys	Glu	Gly	Glu	Glu	Pro	Thr	Val	Tyr	Ser	Asp	Glu	Glu	Glu	Pro	Lys	
				175					180					185			
	GAT	GAG	AGT	GCC	CGG	AAA	AAT	GAT	TAAA	GCAI	TTC A	AGTGG	AAGI	A TA	ATCTA	ΑT	690
	Asp	Glu	Ser	Ala	Arg	Lys	Asn	Asp									
25			190					195									
	TTTT	GTA	rtt 1	rgca/	AAATO	A T	rtgt <i>i</i>	AACAG	TCC	CACTO	CTGT	CTTI	AAAA'	CA I	CAGTO	SATTAC	750
	AATA	ATTTA	AGA A	AAGTI	TTGA	G C	ACTTO	CTAT	' AAG	TTTI	ATT	TAAC	CATCA	CT A	AGTGA	CACTA	810
	ATAA	TAAL	CAA (CTTCI	TAGA	A TO	CATO	ATGT	GTI	TGT	TGT	CACA	AATC	CA G	DAAAG	TGAAC	870
	TGCA	GTG	CTG T	TAAT	CACA	AT G	raat 1	CACTG	TTI	TTCI	TOT	ATCI	GTAG	TT A	AGTAC	CAGGAT	930
30	GAAT	ATT?	AAT (STGT	TTTC	C TO	SAGAG	ACAA	GGA	AGAC	CTTG	GGTA	ATTTC	CC A	AAAA	AGGTA	990
	AAAA	ATCT	AA1	ATGTO	CAC	CA AC	GAGCA	AAAGG	ATC	CAACI	TTT	AGTO	CATGA	TG T	TCTC	TAAAG	1050
	ACAA	CAA	ATC (CTT	TTTT	T T	CTCAA	ATTGA	CTI	AACI	CGCA	TGAT	TTCI	GT 1	ratt1	CTACC	1110
	TCTA	AAGG	CAA A	ATCTO	CAGI	G T	CCAA	AGAC	TTI	GGTA	ATGG	ATTA	AGCG	CT G	STCCA	GTAAC	1170
	AAAA	TGA	AAT (CTCAA	AAACA	G A	CTCA	AGCTG	CAA	AAAA	AGCA	TATI	TTCI	GT G	STTTC	TGGAC	1230
35	TGCA	CTG	TTG 1	CCTI	rgcc	T CA	ACATA	AGACA	CTC	AGAC	CACC	CTCA	CAAA	CA C	CAGTA	GTCTA	1290
	TAGT	TAGO	GAT T	AAA1	ATAGG	A TO	CTGAA	CATT	CAA	AAGA	AAG	CTTT	GGAA	AA A	AAAGA	GCTGG	1350
	CTGG	CCTA	AAA A	AACCI	[AAA]	T A	ATGAT	[GAAG	ATI	GTAG	GAC	TGTC	CTTCC	CA A	AGCCC	CATGT	-1410
	TCAT	rggro	agg (CAAT	יתפייו	ית אי	רתכניו	ኮጥልጥፕ	ጥጥል	CTCA	ጥጥል	CCTT	PACTO	TC A	\ ጥ ጥጥር	AAATG	1470

WO 98/55508

140

AGGGAGGGAC ATACAGAATA GGAACAGGTG TTTGCTCTCC TAAGAGCCTT CATGCACACC

CCTGAACCAC GAGGAAACAG TACAGTCGCT AGTCAAGTGG TTTTTAAAGT AAAGTATATT

	CATAAGGTAA CAGTTATTCT GTTGTTATAA AACTATACCC ACTGCAAAAG TAGTAGTCAA	1650
	GTGTCTAGGT CTTTGATATT GCTCTTTTGG TTAACACTAA GCTTAAGTAG ACTATACAGT	1710
5	TGTATGAATT TGTAAAAGTA TATGAACACC TAGTGAGATT TCAAACTTGT AATTGTGGTT	1770
	AAATAGTCAT TGTATTTTCT TGTGAACTGT GTTTTATGAT TTTACCTCAA ATCAGAAAAC	1830
	AAAATGATGT GCTTTGGTCA GTTAATAAAA ATGGTTTTAC CCACT	1875
. 10	(2) INFORMATION FOR SEQ ID NO: 47:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1563	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
15	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
20	(B) CELL KIND: Stomach cancer	
•	(D) CLONE NAME: HP10415	
	(in) CROHENCE CHARACTERICTICS.	
	(ix) SEQUENCE CHARACTERISTICS: (A) CHARACTERIZATION CODE: CDS	
25	(B) EXISTENCE POSITION: 72 1460	
23	(C) CHARACTERIZATION METHOD: E	
	(O) GIMMOTERIZATION RETROD. E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:	
	(112) 32(321) 32(31) 32(31) 32(31)	
30	AAATTGGGCC AGGCTGAGGC GCTGCTGCTG GAGCGGCCGA TCCGAGACGT GGCTCCCTGG	60
	GCGGCAGAAC C ATG TTG GAC TTC GCG ATC TTC GCC GTT ACC TTC TTG CTG	110
	Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu	
	1 5 10	
	GCG TTG GTG GGA GCC GTG CTC TAC CTC TAT CCG GCT TCC AGA CAA GCT	158
35	Ala Leu Val Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala	
	15 20 25	
	GCA GGA ATT CCA GGG ATT ACT CCA ACT GAA GAA AAA GAT GGT AAT CTT	206
	Ala Gly Ile Pro Gly Ile Thr Pro Thr Glu Glu Lys Asp Gly Asp Leu	

PCT/JP98/02445

1530

	30					35					40					45	
	CCA	GAT	ATT	GTG	AAT	AGT	GGA	AGT	TTG	CAT	GAG	TTC	CTG	GTT	AAT	TTG	254
	Pro	Asp	Ile	Val	Asn	Ser	Gly	Ser	Leu	His	Glu	Phe	Leu	Va1	Asn	Leu	
					50					55					60		
5	CAT	GAG	AGA	TAT	GGG	CCT	GTG	GTC	TCC	TTC	TGG	TTT	GGC	AGG	CGC	CTC	302
	His	Glu	Arg	Tyr	Gly	Pro	Val	Val	Ser	Phe	Trp	Phe	Gly	Arg	Arg	Leu	
				65					70					75			
	GTG	GTT	AGT	TTG	GGC	ACT	GTT	GAT	GTA	CTG	AAG	CAG	CAT	ATC	AAT	CCC	350
	Val	Val	Ser	Leu	Gly	Thr	Val	Asp	Val	Leu	Lys	Gln	His	Ile	Asn	Pro	
10			80					85					90				
	AAT	AAG	ACA	TTG	GAC	CCT	TTT	GAA	ACC	ATG	CTG	AAG	TCA	TTA	TTA	AGG	398
	Asn	Lys	Thr	Leu	Asp	Pro	Phe	Glu	Thr	Met	Leu	Lys	Ser	Leu	Leu	Arg	
		95					100					105					
	TAT	CAA	TCT	GGT	GGT	GGC	AGT	GTG	AGT	GAA	AAC	CAC	ATG	AGG	AAA	AAA	446
15	Tyr	Gln	Ser	Gly	Gly	Gly	Ser	Val	Ser	Glu	Asn	His	Met	Arg	Lys	Lys	
	110					115					120					125	
	TTG	TAT	GAA	AAT	GGT	GTG	ACT	GAT	TCT	CTG	AAG	AGT	AAC	TTT	GCC	CTC	494
	Leu	Tyr	Glu	Asn	Gly	Val	Thr	Asp	Ser	Leu	Lys	Ser	Asn	Phe	Ala	Leu	
					130					135					140		
20	CTC	CTA	AAG	CTT	TCA	GAA	GAA	TTA	TTA	GAT	AAA	TGG	CTC	TCC	TAC	CCA	542
	Leu	Leu	Lys	Leu	Ser	Glu	Glu	Leu	Leu	Asp	Lys	Trp	Leu	Ser	Tyr	Pro	
				145					150					155			
	GAG	ACC	CAG	CAC	GTG	CCC	CTC	AGC	CAG	CAT	ATG	CTT	GGT	TTT	GCT	ATG	590
	Glu	Thr	Gln	His	Val	Pro	Leu	Ser	Gln	His	Met	Leu	Gly	Phe	Ala	Met	
25			160					165					170				
	AAG	TCT	GTT	ACA	CAG	ATG	GTA	ATG	GGT	AGT	ACA	TTT	GAA	GAT	GAT	CAG	638
	Lys	Ser	Val	Thr	Gln	Met	Val	Met	Gly	Ser	Thr	Phe	Glu	Asp	Asp	Gln	
		175					180					185					
															GAG		686
30	Glu	Val	Ile	Arg	Phe	Gln	Lys	Asn	His	Gly	Thr	Val	Trp	Ser	Glu		
	190					195					200					205	
															CGG		734
	Gly	Lys	Gly	Phe		Asp	Gly	Ser	Leu	_	Lys	Asn	Met	Thr	Arg	Lys	
					210					215					220		
35							-								AGG		782
	Lys	Gln	Tyr		Asp	Ala	Leu	Met		Leu	Glu	Ser	Val		Arg	Asn	
				225			_		230	_				235		A 177 177	
	ATC	ATA	AAA	GAA	CGA	AAA	GGA	AGG	AAC	TTC	AGT	CAA	CAT	ATT	TTC	ATT	830

	Ile	Ile	Lys	Glu	Arg	Lys	Gly	Arg	Asn	Phe	Ser	Gln	His	Ile	Phe	Ile	
			240					245					250				
	GAC	TCC	TTA	GTA	CAA	GGG	AAC	CTT	AAT	GAC	CAA	CAG	ATC	CTA	GAA	GAC	878
	Asp	Ser	Leu	Val	Gln	Gly	Asn	Leu	Asn	Asp	Gln	Gln	Ile	Leu	Glu	Asp	
5		255					260					265					
	AGT	ATG	ATA	TTT	TCT	CTG	GCC	AGT	TGC	ATA	ATA	ACT	GCA	AAA	TTG	TGT	926
	Ser	Met	Ile	Phe	Ser	Leu	Ala	Ser	Cys	Ile	Ile	Thr	Ala	Lys	Leu	Cys	
	270					275					280					285	
	ACC	TGG	GCA	ATC	TGT	TTT	TTA	ACC	ACC	TCT	GAA	GAA	GTT	CAA	AAA	AAA	974
10	Thr	Trp	Ala	Ile	Cys	Phe	Leu	Thr	Thr	Ser	Glu	Glu	Val	Gln	Lys	Lys	
					290					295					300		
	TTA	TAT	GAA	GAG	ATA	AAC	CAA	GTT	TTT	GGA	AAT	GGT	CCT	GTT	ACT	CCA	1022
	Leu	Tyr	Glu	Glu	Ile	Asn	Gln	Val	Phe	Gly	Asn	Gly	Pro	Val	Thr	Pro	
				305					310					315			
15	GAG	AAA	ATT	GAG	CAG	CTC	AGA	TAT	TGT	CAG	CAT	GTG	CTT	TGT	GAA	ACT	1070
	Glu	Lys	Ile	Glu	Gln	Leu	Arg	Tyr	Cys	Gln	His	Val	Leu	Cys	Glu	Thr	
			320					325					330				
	GTT	CGA	ACT	GCC	AAA	CTG	ACT	CCA	GTT	TCT	GCC	CAG	CTT	CAA	GAT	ATT	1118
	Val	Arg	Thr	Ala	Lys	Leu	Thr	Pro	Val	Ser	Ala	Gln	Leu	Gln	Asp	Ile	
20		335					340					345					
	GAA	GGA	AAA	ATT	GAC	CGA	TTT	ATT	ATT	CCT	AGA	GAG	ACC	CTC	GTC	CTT	1166
	Glu	Gly	Lys	Ile	Asp	Arg	Phe	Ile	Ile	Pro	Arg	Glu	Thr	Leu	Val	Leu	
	350					355					360					365	
	TAT	GCC	CTT	GGT	GTG	GTA	CTT	CAG	GAT	CCT	AAT	ACT	TGG	CCA	TCT	CCA	1214
25	Tyr	Ala	Leu	Gly	Val	Val	Leu	Gln	Asp	Pro	Asn	Thr	Trp	Pro	Ser	Pro	
					370					375					380		
	CAC	AAG	TTT	GAT	CCA	GAT	CGG	TTT	GAT	GAT	GAA	TTA	GTA	ATG	AAA	ACT	1262
	His	Lys	Phe	Asp	Pro	Asp	Arg	Phe	Asp	Asp	Glu	Leu	Val	Met	Lys	Thr	
				385					390					395			
30	TTT	TCC	TCA	CTT	GGA	TTC	TCA	GGC	ACA	CAG	GAG	TGT	CCA	GAG	TTG	AGG	1310
	Phe	Ser	Ser	Leu	Gly	Phe	Ser	Gly-	Thr	Gln	Glu	Cys	Pro	Glu	Leu	Arg	
			400					405					410				
	TTT	GCA	TAT	ATG	GTG	ACC	ACA	GTA	CTT	CTT	AGT	GTA	TTG	GTG	AAG	AGA	1358
	Phe	Ala	Tyr	Met	Val	Thr	Thr	Val	Leu	Leu	Ser	Val	Leu	Val	Lys	Arg	
35		415					420					425					
	CTG	CAC	CTA	CTT	TCT	GTG	GAG	GGA	CAG	GTT	ATT	GAA	ACA	AAG	TAT	GAA	1406
	Leu	His	Leu	Leu	Ser	Val	Glu	Gly	Gln	Val	Ile	Glu	Thr	Lys	Tyr	Glu	
	430					435					440					445	

	ord or non row how day day dor not be not be non	145
	Leu Val Thr Ser Ser Arg Glu Glu Ala Trp Ile Thr Val Ser Lys Arg	
	450 455 460	
	TAT TAAAATTTTA TACATTTAAA ATCATTGTTA AATTGATTGA GGAAAACAAC CAT	151
5	Tyr	
	TTAAAAAAA TCTATGTTGA ATCCTTTTAT AAACCAGTAT CACTTTGTAA TAT	156
10	(2) INFORMATION FOR SEQ ID NO: 48:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 2030	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
15	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
20	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10419	
	(in) CEOUENGE GHADACHEDIOMICS	
	(ix) SEQUENCE CHARACTERISTICS:	
25	(A) CHARACTERIZATION CODE: CDS	
23	(B) EXISTENCE POSITION: 171 914 (C) CHARACTERIZATION METHOD: E	
	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:	
	(AI) DEGEMENT PRODUCTION. DEG ID No. 40.	
30	CATTTGGGGT TTCGGTTCCC CCCCTTCCCC TTCCCCGGGG TCTGGGGGTG ACATTGCACC	60
	GCGCCCTCG TGGGGTCGCG TTGCCACCCC ACGCGGACTC CCCAGCTGGC GCGCCCCTCC	120
	CATTTGCCTG TCCTGGTCAG GCCCCCACCC CCCTTCCCAC CTGACCAGCC ATG GGG	176
	Met Gly	
	1	
35	GCT GCG GTG TTT TTC GGC TGC ACT TTC GTC GCG TTC GGC CCG GCC TTC	224
	Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro Ala Phe	
	5 10 15	
	GCG CTT TTC TTG ATC ACT GTG GCT GGG GAC CCG CTT CGC GTT ATC ATC	272
	•	

	Ala	Leu	Phe	Leu	Ile	Thr	Val	Ala	Gly	Asp	Pro	Leu	Arg	Val	Ile	Ile	
		20					25					30					
	CTG	GTC	GCA	GGG	GCA	TTT	TTC	TGG	CTG	GTC	TCC	CTG	CTC	CTG	GCC	TCT	320
	Leu	Val	Ala	Gly	Ala	Phe	Phe	Trp	Leu	Val	Ser	Leu	Leu	Leu	Ala	Ser	
5	35					40					45					50 .	
	GTG	GTC	TGG	TTC	ATC	TTG	GTC	CAT	GTG	ACC	GAC	CGG	TCA	GAT	GCC	CGG	368
	Val	Val	Trp	Phe	Ile	Leu	Val	His	Val	Thr	Asp	Arg	Ser	Asp	Ala	Arg	
					55					60					65		
	CTC	CAG	TAC	GGC	CTC	CTG	ATT	TTT	GGT	GCT	GCT	GTC	TCT	GTC	CTT	CTA	416
10	Leu	Gln	Tyr	Gly	Leu	Leu	Ile	Phe	Gly	Ala	Ala	Val	Ser	Val	Leu	Leu	
				70					75					80			
	CAG	GAG	GTG	TTC	CGC	TTT	GCC	TAC	TAC	AAG	CTG	CTT	AAG	AAG	GCA	GAT	464
	Gln	Glu	Val	Phe	Arg	Phe	Ala	Tyr	Tyr	Lys	Leu	Leu	Lys	Lys	Ala	Asp	
			85					90					95				
15	GAG	GGG	TTA	GCA	TCG	CTG	AGT	GAG	GAC	GGA	AGA	TCA	CCC	ATC	TCC	ATC	512
	Glu	Gly	Leu	Ala	Ser	Leu	Ser	Glu	Asp	Gly	Arg	Ser	Pro	Ile	Ser	Ile	
		100					105					110					
	CGC	CAG	ATG	GCC	TAT	GTT	TCT	GGT	CTC	TCC	TTC	GGT	ATC	ATC	AGT	GGT	560
	Arg	Gln	Met	Ala	Tyr	Val	Ser	Gly	Leu	Ser	Phe	Gly	Ile	Ile	Ser	Gly	
20	115					120					125					130	
	GTC	TTC	TCT	GTT	ATC	AAT	ATT	TTG	GCT	GAT	GCA	CTT	GGG	CCA	GGT	GTG	608
	Val	Phe	Ser	Val	Ile	Asn	Ile	Leu	Ala	Asp	Ala	Leu	Gly	Pro	Gly	Val	
					135					140					145		
	GTT	GGG	ATC	CAT	GGA	GAC	TCA	CCC	TAT	TAC	TTC	CTG	ACT	TCA	GCC	TTT	656
25	Val	Gly	Ile	His	Gly	Asp	Ser	Pro	Tyr	Tyr	Phe	Leu	Thr	Ser	Ala	Phe	
				150					155					160			
	CTG	ACA	GCA	GCC	ATT	ATC	CTG	CTC	CAT	ACC	TTT	TGG	GGA	GTT	GTG	TTC	704
	Leu	Thr	Ala	Ala	Ile	Ile	Leu	Leu	His	Thr	Phe	Trp	Gly	Val	Val	Phe	
			165					170					175				
30	TTT	GAT	GCC	TGT	GAG	AGG	AGA	CGG	TAC	TGG	GCT	TTG	GGC	CTG	GTG	GTT	752
	Phe	Asp	Ala	Cys	Glu	Arg	Arg	Arg	Tyr	Trp	Ala	Leu	Gly	Leu	Val	Val	
		180					185					190					
	GGG	AGT	CAC	CTA	CTG	ACA	TCG	GGA	CTG	ACA	TTC	CTG	AAC	ccc	TGG	TAT	800
	Gly	Ser	His	Leu	Leu	Thr	Ser	Gly	Leu	Thr	Phe	Leu	Asn	Pro	Trp	Tyr	
35	195					200					205					210	
	GAG	GCC	AGC	CTG	CTG	CCC	ATC	TAT	GCA	GTC	ACT	GTT	TCC	ATG	GGG	CTC	848
	Glu	Ala	Ser	Leu	Leu	Pro	Ile	Tyr	Ala	Val	Thr	Val	Ser	Met	Gly	Leu	
					215					220					225		

145

	TGG GCC TTC ATC ACA GCT GGA GGG TCC CTC CGA AGT ATT CAG CGC AGC	896
	Trp Ala Phe Ile Thr Ala Gly Gly Ser Leu Arg Ser Ile Gln Arg Ser	
	230 235 240	
	CTC TTG TGT AAG GAC TGACTACCTG GACTGATCGC CTGACAGATC CCACCTGCC	950
5	Leu Leu Cys Lys Asp	
	245	
	TGTCCACTGC CCATGACTGA GCCCAGCCCC AGCCCGGGTC CATTGCCCAC ATTCTCTGTC	1010
	TCCTTCTCGT CGGTCTACCC CACTACCTCC AGGGTTTTGC TTTGTCCTTT TGTGACCGTT	1070
	AGTCTCTAAG CTTTACCAGG AGCAGCCTGG GTTCAGCCAG TCAGTGACTG GTGGGTTTGA	1130
10	ATCTGCACTT ATCCCCACCA CCTGGGGACC CCCTTGTTGT GTCCAGGACT CCCCCTGTGT	1190
	CAGTGCTCTG CTCTCACCCT GCCCAAGACT CACCTCCCTT CCCCTCTGCA GGCCGACGGC	1250
	AGGAGGACAG TCGGGTGATG GTGTATTCTG CCCTGCGCAT CCCACCCGAG GACTGAGGGA	1310
	ACCTAGGGGG GACCCCTGGG CCTGGGGTGC CCTCCTGATG TCCTCGCCCT GTATTTCTCC	1370
	ATCTCCAGTT CTGGACAGTG CAGGTTGCCA AGAAAAGGGA CCTAGTTTAG CCATTGCCCT	1430
15	GGAGATGAAA TTAATGGAGG CTCAAGGATA GATGAGCTCT GAGTTTCTCA GTACTCCCTC	1490
	AAGACTGGAC ATCTTGGTCT TTTTCTCAGG CCTGAGGGGG AACCATTTTT GGTGTGATAA	1550
	ATACCCTAAA CTGCCTTTTT TTCTTTTTTG AGGTGGGGG AGGGAGGAGG TATATTGGAA	1610
	CTCTTCTAAC CTCCTTGGGC TATATTTTCT CTCCTCGAGT TGCTCCTCAT GGCTGGGCTC	1670
	ATTTCGGTCC CTTTCTCCTT GGTCCCAGAC CTTGGGGGAA AGGAAGGAAG TGCATGTTTG	1730
20	GGAACTGGCA TTACTGGAAC TAATGGTTTT AACCTCCTTA ACCACCAGCA TCCCTCCTCT	1790
	CCCCAAGGTG AAGTGGAGGG TGCTGTGGTG AGCTGGCCAC TCCAGAGCTG CAGTGCCACT	1850
	GGAGGAGTCA GACTACCATG ACATCGTAGG GAAGGAGGGG AGATTTTTTT GTAGTTTTTA	1910
	ATTGGGGTGT GGGAGGGCG GGGAGGTTTT CTATAAACTG TATCATTTTC TGCTGAGGGT	1970
	GGAGTGTCCC ATCCTTTTAA TCAAGGTGAT TGTGATTTTG ACTAATAAAA AAGAATTTGT	2030
25		
	(2) INFORMATION FOR SEQ ID NO: 49:	

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 493
- (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
- 35 (vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP10424

										146							
		(ix)	SEQU	ENCE	СНА	RACT	ERIS	TICS	:							
				(A)	CHA	RACT	ERIZ	ATIO	и со	DE:	CDS						
				(B)	EXI	STEN	CE P	OSIT	ION:	98.	. 43	9					
				(C)	СНА	RACT	ERIZ	ATIO	N ME	THOD	: E						
5																	
		(:	xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	49:					
	AAA	GTTT	CCC .	AAAT	CCAG	GC G	GCTA	GAGG	C CC.	ACTG	CTTC	CCA	ACTA	CCA	GCTG	AGGGG	G 60
	TCC	GTCC	CGA	GAAG(GGAG.	AA G.	AGGC	CGAA	G AG	GAAA	C AT	G AA	C TT	C TA	T TT	A CTC	115
10													n Ph	е Ту		u Leu	
	0.5	000										1				5	
				AGC													163
	Leu	AIA	ser	Ser	TIE	Leu	Cys	ALA		Ile	Val	Phe	Trp		Tyr	Arg	
15	ccc	ጥጥጥ	CAC	10	440	4 C TD	000	044	15	ma .			ma.	20	0.05	0.00m	
13				AGA													211
	nig	rne	25	Arg	ASII	inr	GIY		met	Ser	Ser	Asn		Inr	ALB	Leu	
	CCA	ርጥ ለ		AGA	ccc	ጥረጥ	mcm	30	000	mm A	4 m m	440	35	4 A TT	404	C 4 C	250
																	259
20	mia	40	V & I	Arg	110	per	45	261	GLY	Leu	116	50	261	ASII	1111	veh	
20	AAC		СТТ	GCA	GTC	TAC		СТС	ጥርጥ	CGG	CAT		ጥጥΔ	ΔΔΨ	ΔΔΤ	ጥጥር	307
				Ala													307
	55				,,,	60	р	200	501	B	65	110	Deu	11511	11511	70	
		CAC	TCA	ATA	GCC		CAG	AAG	CGA	АТА		СТА	AAC	СТС	AGT		355
25				Ile													333
					75			_, -		80					85		
	GTG	GAA	AAC	AAG	CTG	GTT	GAA	CTG	GAA		ACT	CTA	CTT	AGC		GGT	403
				Lys													
				90					0.5					100	•	•	

30 TTC AGA GGT GCA TCA CCT CAC CGG AAA TCC ACC TAAAAGCGTA CAGG 450 Phe Arg Gly Ala Ser Pro His Arg Lys Ser Thr 110

ATGTAATGCC AGTGGTGGAA ATCATTAAAG ACACTTTGA GTAG 493

35

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2044

				(B)	TYP	E: N	ucle	ic a	cid								
				(C)	STR	ANDE	DNES	S: D	oubl	е							
				(D)	TOP	OLOG'	Y: L	inea	r								
		(ii)	SEQU	ENCE	KIN	D: c	DNA	to m	RNA							
5																	
		(vi)	ORIG	INAL	SOU	RCE:										
				(A)	ORG.	ANIS	M: <i>H</i>	ото	sapi	ens							
				(B)	CEL	L KI	ND:	Epid	ermo	id c	arci	noma					
				(C)	CEL	L LI	NE:	KВ									
10				(D)	CLO	NE N	AME:	HP1	0428								
		(ix)	SEQU:	ENCE	CHA	RACT	ERIS	TICS	:							
				(A)	CHA	RACT	ERIZ	ATIO	N CO	DE:	CDS						
				(B)	EXI	STEN	CE P	OSIT	ION:	288	1	385					
15				(C)	CHA	RACT	ERIZ	ATIO	N ME	THOD	: E						
		(:	xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	50:					
	AGA'	TTCC	GGC	CTGG	AGCT	CC C	AGGG	CCGA	G CA	GACC'	TTGG	GAC	CTGT	GAG	CGCT	GCATCC	60
20	AAT'	TAAC	CAT (GGGA	AGGG'	TC A	GCAC	CAGC	CAC	CAGC	CCCT	TAG	GTGA	GGA	CTCT	GCCTGG	120
	GGC'	rctg(CTG .	ATGG'	TTCC	GA A	rcat(GGAG	C TG	CAGA	GAGC	TCC'	rcca(GCC	TGGA	GACGTT	180
	CTT	GGTG	AAA (GCTG'	IGGT(CT A	ACTC	CACC	G GC'	TCTT(CCTG	CAC	ATTG'	TAT	TCAA	GAGGGG	240
	TGC	CTGC	CCC	CGCT	GACT	CA G	GAGC'	TCCG	G TG	CTGC	AGCC	GCC	ACGA	ATG	GGG	AGG	296
														Met	Gly	Arg	
25														1			
	TGG	GCC	CTC	GAT	GTG	GCC	TTT	TTG	TGG	AAG	GCG	GTG	TTG	ACC	CTG	GGG	344
	Trp	Ala	Leu	Asp	Val	Ala	Phe	Leu	Trp	Lys	Ala	Val	Leu	Thr	Leu	Gly	
		5					10					15					
	CTG	GTG	CTT	CTC	TAC	TAC	TGC	TTC	TCC	ATC	GGC	ATC	ACC	TTC	TAC	AAC	392
30	Leu	Val	Leu	Leu	Tyr	Tyr	Cys	Phe	Ser	Ile	Gly	Ile	Thr	Phe	Tyr	Asn	
	20					25					30					35	
	AAG	TGG	CTG	ACA	AAG	AGC	TTC	CAT	TTC	CCC	CTC	TTC	ATG	ACG	ATG	CTG	440
	Lys	Trp	Leu	Thr	Lys	Ser	Phe	His	Phe	Pro	Leu	Phe	Met	Thr	Met	Leu	
					40					45					50		
35	CAC	CTG	GCC	GTG	ATC	TTC	CTC	TTC	TCC	GCC	CTG	TCC	AGG	GCG	CTG	GTT	488
	His	Leu	Ala	Val	Ile	Phe	Leu	Phe	Ser	Ala	Leu	Ser	Arg	Ala	Leu	Val	
				55					60					65			
	CAG	TGC	TCC	AGC	CAC	AGG	GCC	CGT	GTG	GTG	CTG	AGC	TGG	GCC	GAC	TAC	536

	Gln	Cys	Ser 70	Ser	His	Arg	Ala	Arg 75	Val	Val	Leu	Ser	Trp 80	Ala	Asp	Tyr	
	CTC	AGA	AGA	GTG	GCT	CCC	ACA	GCT	CTG	GCG	ACG	GCG	CTT	GAC	GTG	GGC	584
	Leu	Arg	Arg	Val	Ala	Pro	Thr	Ala	Leu	Ala	Thr	Ala	Leu	Asp	Val	Gly	
5		85					90					95					
	TTG	TCC	AAC	TGG	AGC	TTC	CTG	TAT	GTC	ACC	GTC	TCG	CTG	TAC	ACA	ATG	632
	Leu	Ser	Asn	Trp	Ser	Phe	Leu	Tyr	Val	Thr	Val	Ser	Leu	Tyr	Thr	Met	
	100					105					110					115	
	ACC	AAA	TCC	TCA	GCT	GTC	CTC	TTC	ATC	TTG	ATC	TTC	TCT	CTG	ATC	TTC	680
10	Thr	Lys	Ser	Ser	Ala	Val	Leu	Phe	Ile	Leu	Ile	Phe	Ser	Leu	Ile	Phe	
					120					125					130		
•	AAG	CTG	GAG	GAG	CTG	CGC	GCG	GCA	CTG	GTC	CTG	GTG	GTC	CTC	CTC	ATC	728
	Lys	Leu	Glu	Glu	Leu	Arg	Ala	Ala	Leu	Val	Leu	Val	Val	Leu	Leu	Ile	
				135					140					145			
15	GCC	GGG	GGT	CTC	TTC	ATG	TTC	ACC	TAC	AAG	TCC	ACA	CAG	TTC	AAC	GTG	776
	Ala	Gly	Gly	Leu	Phe	Met	Phe	Thr	Tyr	Lys	Ser	Thr	Gln	Phe	Asn	Val	
			150					155					160				
	GAG	GGC	TTC	GCC	TTG	GTG	CTG	GGG	GCC	TCG	TTC	ATC	GGT	GGC	ATT	CGC	824
	Glu	G1y	Phe	Ala	Leu	Val	Leu	Gly	Ala	Ser	Phe	Ile	Gly	Gly	Ile	Arg	
20		165					170					175					
	TGG	ACC	CTC	ACC	CAG	ATG	CTC	CTG	CAG	AAG	GCT	GAA	CTC	GGC	CTC	CAG	872
	Trp	Thr	Leu	Thr	Gln	Met	Leu	Leu	Gln	Lys	Ala	Glu	Leu	Gly	Leu	Gln	
	180					185					190					195	
	AAT	CCC	ATC	GAC	ACC	ATG	TTC	CAC	CTG	CAG	CCA	CTC	ATG	TTC	CTG	GGG	920
25	Asn	Pro	Ile	Asp	Thr	Met	Phe	His	Leu	Gln	Pro	Leu	Met	Phe	Leu	Gly	
					200					205					210		
	CTC	TTC	CCT	CTC	TTT	GCT	GTA	TTT	GAA	GGT	CTC	CAT	TTG	TCC	ACA	TCT	968
	Leu	Phe	Pro	Leu	Phe	Ala	Val	Phe	Glu	Gly	Leu	His	Leu	Ser	Thr	Ser	
				215					220					225			
30	GAG	AAA	ATC	TTC	CGT	TTC	CAG	GAC	ACA	GGG	CTG	CTC	CTG	CGG	GTA	CTT	1016
•	Glu	Lys	Ile	Phe	Arg	Phe	Gln	Asp	Thr	Gly	Leu	Leu	Leu	Arg	Val	Leu	
			230					235					240				
	GGG	AGC	CTC	TTC	CTT	GGC	GGG	ATT	CTC	GCC	TTT	GGT	TTG	GGC	TTC	TCT	1064
	Gly	Ser	Leu	Phe	Leu	Gly	Gly	Ile	Leu	Ala	Phe	Gly	Leu	G1y	Phe	Ser	
35		245				_	250					255					
•	GAG	TTC	CTC	CTG	GTC	TCC	AGA	ACC	TCC	AGC	CTC	ACT	CTC	TCC	ATT	GCC	1112
	Glu	Phe	Leu	Leu	Val	Ser	Arg	Thr	Ser	Ser	Leu	Thr	Leu	Ser	Ile	Ala	
	260					265					270					275	

149

	GGC	ATT	TTT	AAG	GAA	GTC	TGC	ACT	TTG	CTG	TTG	GCA	GCT	CAT	CTG	CTG	1160
	Gly	Ile	Phe	Lys	Glu	Val	Cys	Thr	Leu	Leu	Leu	Ala	Ala	His	Leu	Leu	
					280					285					290		
	GGC	GAT	CAG	ATC	AGC	CTC	CTG	AAC	TGG	CTG	GGC	TTC	GCC	CTC	TGC	CTC	1208
5	Gly	Asp	Gln	Ile	Ser	Leu	Leu	Asn	Trp	Leu	G1y	Phe	Ala	Leu	Cys	Leu	
				295					300					305			
	TCG	GGA	ATA	TCC	CTC	CAC	GTT	GCC	CTC	AAA	GCC	CTG	CAT	TCC	AGA	GGT	1256
	Ser	Gly	Ile	Ser	Leu	His	Val	Ala	Leu	Lys	Ala	Leu	His	Ser	Arg	Gly	
			310					315					320				
10	GAT	GGT	GGC	CCC	AAG	GCC	TTG	AAG	GGG	CTG	GGC	TCC	AGC	CCC	GAC	CTG	1304
	Asp	Gly	Gly	Pro	Lys	Ala	Leu	Lys	Gly	Leu	Gly	Ser	Ser	Pro	Asp	Leu	
		325					330					335					•
	GAG	CTG	CTG	CTC	CGG	AGC	AGĊ	CAG	CGG	GAG	GAA	GGT	GAC	TAA	GAG	GAG	1352
	Glu	Leu	Leu	Leu	Arg	Ser	Ser	Gln	Arg	Glu	Glu	Gly	Asp	Asn	Glu	Glu	
15	340					345					350					355	
	GAG	GAG	TAC	TTT	GTG	GCC	CAG	GGG	CAG	CAG	TGAC	CCAG	CA C	GGC#	TAAA		1400
	Glu	Glu	Tyr	Phe	Val	Ala	Gln	Gly	Gln	Gln						•	
					360					365							
	GGC	TAGA	AAG (CAGGC	CACT	C C	CCAGC	CTGC	TGC	CAGC	CACT	CACT	GTGC	TC A	AGCC	GCCAG	1460
20	GGC	CATO	CAT	GGTAG	CTG	G A	CTGT	'GGAC	GGG	AGTO	CACC	AGGT	GGTG	GG G	CCAA	GCCAG	1520
	GGA	CTCAT	rga (CTTTI	rgccc	CC TO	CCTI	CAGA	GCC	TGGT	CAC	ACAA	GGGG	CG A	AGCAC	CAGGC	1580
	CAG	CTG	GGA (CTGGC	CAGA	AG C	rgggc	CCAA	GCI	GCGC	TGG	AATO	GCAG	CA G	GAGA	GGGGA	1640
	GTG	GCT	GT 1	TCTTC	CCAC	CC AC	CTTCC	CAGG	CTC	TGAC	CAGC	CGAG	ACTO	TA:	TCCA	LAGGCA	1700
	CAGO	CAGC	TTT (CTAAA	AGGGA	C TO	AGT1	TGGA	CTG	GGTI	TTG	GACC	TCCA	GG G	GCTG	GAGCT	1760
25	TCAT	CACC	CTG (GGCAG	TGTC	T T	TCTC	CAGAG	AGC	AGGI	TTC	TTTA	TAG1	TT G	GAAA	TAAAT	1820
	GGTT	CACG	GT (CCACI	rggcc	G C	TTGT	GTTG	CTG	GAGA	CGT	GGGG	GCAG	GG A	GGGG	ACAGT	1880
																TCTTA	1940
														cc c	CAGI	GGGGC	2000
	CCCA	CTGC	CAC (CTGCI	rggca	G GA	AAATA	AATG	AAT	GTTI	ACT	GAGI	•				2044
30																	

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1043

35 (B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

150

(vi) ORIGINAL SOURCE:

				(A)	ORG	ANISI	M: H	ото	sapi	ens							
				(B)	CEL	L KI	ND:	Stom	ach (canc	er '						
				(D)	CLO	NE N	AME:	HP1	0429								
5																	
		(ix)	SEQU	ENCE	CHA	RACT	ERIS'	TICS	:							
				(A)	CHA	RACT	ERIZ	ATIO	N CO	DE:	CDS						
				(B)	EXI	STEN	CE P	OSIT	ION:	157	8	37					
				(C)	CHA	RACT	ERIZ	ATIO	N ME	THOD	: E						
10															•		
		(:	xi)	SEQU	ENCE	DES	CRIP'	TION	: SE	QID	NO:	51:					
•									,								
																TTAGAC	60
1.5																ATATTC	120
15	CTT	1111	TGT	CCTA	3AGA1	AC I	IATT	rrcc	r Gro	JAAA							174
											Met 1	PIO	IIII	1111	Lys 5	пуs	
	ACA	ጥጥር	ΑТС	TTC	ጥጥΔ	ТСΔ	AGC	ጥጥጥ	ጥጥር	ACC		ርጥጥ	GGG	TCC		Α ጥጥ	222
				Phe													
20				10					15			200	01)	20			
	GTA	ATT	TGC	TCT	ATT	CTT	GGG	ACA		GCA	TGG	ATC	ACC	AGT	ACA	ATT	270
	Val	Ile	Cys	Ser	Ile	Leu	Gly	Thr	Gln	Ala	Trp	Ile	Thr	Ser	Thr	Ile	
			25					30					35				
	GCT	GTT	AGA	GAC	TCT	GCT	TCA	AAT	GGG	AGC	ATT	TTC	ATC	ACT	TAC	GGA	318
25	Ala	Val	Arg	Asp	Ser	Ala	Ser	Asn	Gly	Ser	Ile	Phe	Ile	Thr	Tyr	Gly	
		40					45					50					
	CTT	TTT	CGT	GGG	GAG	AGT	AGT	GAA	GAA	TTG	AGT	CAC	GGA	CTT	GCA	GAA	366
	Leu	Phe	Arg	Gly	Glu	Ser	Ser	Glu	Glu	Leu	Ser	His	Gly	Leu	Ala	Glu	
	55					60					65		٠			70	
30	CCA	AAG	AAA	AAG	TTT	GCA	GTT	TTA	GAG	ATA	CTG	AAT	AAT	TCT	TCC	CAA	414
	Pro	Lys	Lys	Lys	Phe	Ala	Val	Leu	Glu	Ile	Leu	Asn	Asn	Ser		Gln	
				-	75					80					85		
				CAT													462
25	гуs	Thr	Leu	His	Ser	Val	Thr	Ile		Phe	Leu	Val	Leu		Leu	IIe	
35		TCC	CTC	90		m c m	000	mmm	95	mmc	m A C	440	400	100		440	510
				CTG Leu													510
	1114	Der	105	neu	261	Per	GIY	110	IIII	FIIE	TAT	veli	115	116	ner	12011	•
			-00					T T U					J. J. J				

151

	CCT	TAC	CAG	ACA	TTC	CTG	GGG	CCG	ACG	GGG	GTG	TAC	ACC	TGG	AAC	GGG	558
	Pro	Tyr	Gln	Thr	Phe	Leu	Gly	Pro	Thr	Gly	Val	Tyr	Thr	Trp	Asn	Gly	
		120					125					130					
	CTC	GGT	GCA	TCC	TTC	GTT	TTT	GTG	ACC	ATG	ATA	CTG	TTT	GTG	GCG	AAC	606
5	Leu	Gly	Ala	Ser	Phe	Val	Phe	Val	Thr	Met	Ile	Leu	Phe	Val	Ala	Asn	
	135					140					145					150	
	ACG	CAG	TCC	AAC	CAA	CTC	TCC	GAA	GAG	TTG	TTC	CAA	ATG	CTT	TAC	CCG	654
	Thr	Gln	Ser	Asn	Gln	Leu	Ser	Glu	Glu	Leu	Phe	Gln	Met	Leu	Tyr	Pro	
					155					160					165		
10	GCA	ACC	ACC	AGT	AAA	GGA	ACG	ACC	CAC	AGT	TAC	GGA	TAC	TCG	TTC	TGG	702
	Ala	Thr	Thr	Ser	Lys	Gly	Thr	Thr	His	Ser	Tyr	Gly	Tyr	Ser	Phe	Trp	
				170					175					180			
	CTC	ATA	CTG	CTC	GTC	ATT	CTT	CTA	AAT	ATA	GTC	ACT	GTA	ACC	ATC	ATC	750
	Leu	Ile	Leu	Leu	Va1	Ile	Leu	Leu	Asn	Ile	Val	Thr	Val	Thr	Ile	Ile	
15			185					190					195				
	ATT	TTC	TAC	CAG	AAG	GCC	AGA	TAC	CAG	CGG	AAG	CAG	GAG	CAG	AGA	AAG	798
	Ile	Phe	Tyr	Gln	Lys	Ala	Arg	Tyr	Gln	Arg	Lys	Gln	Glu	Gln	Arg	Lys	
		200					205					210					
	CCA	ATG	GAA	TAT	GCT	CCA	AGG	GAC	GGA	ATT	TTA	TTC	TGAA	TTC	CT 1	TCATC	850
20	Pro	Met	Glu	Tyr	Ala	Pro	Arg	Asp	Gly	Ile	Leu	Phe					
	215					220					225						
	TCAT	TTTT	GC G	STTGO	CATC	TA T	GTAC	CATCA	GCC	CTGA	GTA	GTAA	ACTGG	TT A	AGCTI	CTCTG	910
	GACA	ATTO	CAG (CATGO	CAAT	G TO	ACTO	TCAT	CTC	TGAC	CAGC	ATTI	rgtgi	TT C	CATGA	CACTG	970
	TGTT	CTTC	CAT	rgato	CTG1	CA CI	CCTC	AAAA	YTT	TTCC	CAC	AAG	TTGG	GG A	AAATG	SAATGG	1030
25	GAAA	ATGTO	CGC 1	rgg													1043
																•	

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 972

- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: cDNA to mRNA

35

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Liver

152

(D) CLONE NAME: HP10432

(ix) SEQUENCE CHARACTERISTICS:

5

- (A) CHARACTERIZATION CODE: CDS
- (B) EXISTENCE POSITION: 29.. 418
 - (C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

• •																	
10	AGACA	.GCG	GC G	GGCC	CAG	GA CO	STGCA										52
								ľ		Ala A	Arg	Gly		Leu	Arg	Arg	
	mmc	mc.	000	CTI C	CTIC.	C TI C	CMC	000	1	mcc.	C M C	000	5	C TO C	ccc	TCC	100
	TTG C																100
15	Leu L	10	ALG	Leu	Leu	ART	15	GIY	Leu	11p	Leu	20		Leu	ALE	261	
13	GTG G		GGG	GAG	$C\Delta\Delta$	GCG		GGC	۸۵۵	ccc	ccc			ccc	GGC	AGC	148
	Val A																140
	25	.+ 0	Gly	Gru	GIII	30	TIO	Gly	1111	VIG	35	Oys	361	n. R	019	40	
	TCC T	GG	AGC	GCG	GAC		GAC	AAG	TGC	ATG		тес	GCG	тст	TGC		196
20	Ser T																
					45			-, -	-,-	50		٠,٠			55		
	GCG C	GA	CCG	CAC	AGC	GAC	TTC	TGC	CTG		TGC	GCT	GCA	GCA	CCT	CCT	244
	Ala A	rg	Pro	His	Ser	Asp	Phe	Cys	Leu	Gly	Cys	Ala	Ala	Ala	Pro	Pro	
		-		60		_		·	65	•	•			70			
25	GCC C	СС	TTC	CGG	CTG	CTT	TGG	CCC	ATC	CTT	GGG	GGC	GCT	CTG	AGC	CTG	292
	Ala P	ro	Phe	Arg	Leu	Leu	Trp	Pro	Ile	Leu	Gly	Gly	Ala	Leu	Ser	Leu	
			75					80					85				
	ACC T	TC	GTG	CTG	GGG	CTG	CTT	TCT	GGC	TTT	TTG	GTC	TGG	AGA	CGA	TGC	340
	Thr P	he	Val	Leu	Gly	Leu	Leu	Ser	Gly	Phe	Leu	Val	Trp	Arg	Arg	Cys	
30		90					95					100					
	CGC A	GG	AGA	GAG	AAG	TTC	ACC	ACC	ccc	ATA	GAG	GAG	ACC	GGC	GGA	GAG	388
	Arg A	rg	Arg	Glu	Lys	Phe	Thr	Thr	Pro	Ile	Glu	Glu	Thr	Gly	Gly	Glu	
	105					110					115					120	
	GGC T	GC	CCA	GCT	GTG	GCG	CTG	ATC	CAG	TGA	CA A	TGT	GCCC	CCTG	CC A	CCGG	440
35	Gly C	уs	Pro	Ala	Val	Ala	Leu	Ile	Gln								
					125												
	GGCTC	GCC	CA C	CTCAT	CAT	C A	TCAT	CCA	TC	raga	GCCA	GTC	TCTG	CCT	CCCA	GACGCG	500
	GCGGG.	AGC	CA A	GCT	CTC	CA AC	CCACA	AAGGG	GGG	GTGG(GGGG	CGG	TGAA	TCA	CCTC	TGAGGC	560

153

620

CTGGGCCCAG GGTTCAGGGG AACCTTCCAA GGTGTCTGGT TGCCCTGCCT CTGGCTCCAG

	AACAGAAAGG GAGCCTCACG CTGGCTCACA CAAAACAGCT GACACTGACT AAGGAACTGC	680
	AGCATTTGCA CAGGGGAGGG GGGTGCCCTC CTTCCTAGAG GCCCTGGGGG CCAGGCTGAC	740
	TTGGGGGGCA GACTTGACAC TAGGCCCCAC TCACTCAGAT GTCCTGAAAT TCCACCACGG	800
5	GGGTCACCCT GGGGGGTTAG GGACCTATTT TTAACACTAG GGGGCTGGCC CACTAGGAGG	860
	GCTGGCCCTA AGATACAGAC CCCCCAACT CCCCAAAGCG GGGAGGAGAT ATTTATTTTG	920
	GGGAGAGTTT GGAGGGGAGG GAGAATTTAT TAATAAAAGA ATCTTTAACT TT	972
10	(2) INFORMATION FOR SEQ ID NO: 53:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 695	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
15	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
20	(B) CELL KIND: Liver	
	(C) CELL LINE:	
	(D) CLONE NAME: HP10433	
	() OPONENCE ON A DAGE PROTOCIO	
25	(ix) SEQUENCE CHARACTERISTICS:	
25	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 73 564 (C) CHARACTERIZATION METHOD: E	
	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:	
30	(x1) badeaned babonii iton. bad ib no. 55.	
	AAGATTTCAG CTGCGGGACG GTCAGGGGAA ACCTCCAGGC GCAGGGAAGG ACGGCCAGGG	60
	TGACACGGAA GC ATG CGA CGG CTG CTG ATC CCT CTG GCC CTG TGG CTG GGC	111
	Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly	
	1 5 10	
35	GCG GTG GGC GTC GCC GAG CTC ACG GAA GCC CAG CGC CGG GGC	159
	Ala Val Gly Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Arg Gly	
	15 20 25	
	CTG CAG GTG GCC CTG GAG GAA TTT CAC AAG CAC CCG CCC GTG CAG TGG	207

154

	Leu	Gln	Val	Ala	Leu	Glu	Glu	Phe	His	Lys	His	Pro	Pro	Val	Gln	Trp	
	30					35					40					45	
	GCC	TTC	CAG	GAG	ACC	AGT	GTG	GAG	AGC	GCC	GTG	GAC	ACG	CCC	TTC	CCA	255
	Ala	Phe	Gln	Glu	Thr	Ser	Val	Glu	Ser	Ala	Val	Asp	Thr	Pro	Phe	Pro	
5					50					55					60		
	GCT	GGA	ATA	TTT	GTG	AGG	CTG	GAA	TTT	AAG	CTG	CAG	CAG	ACA	AGC	TGC	303
	Ala	Gly	Ile	Phe	Val	Arg	Leu	Glu	Phe	Lys	Leu	Gln	Gln	Thr	Ser	Cys	
				65					70					75			
	CGG	AAG	AGG	GAC	TGG	AAG	AAA	CCC	GAG	TGC	AAA	GTC	AGG	CCC	AAT	GGG	351
10	Arg	Lys	Arg	Asp	Trp	Lys	Lys	Pro	Glu	Cys	Lys	Val	Arg	Pro	Asn	Gly	
			80					85		•			90				
														GAG			399
	Arg	Lys	Arg	Lys	Cys	Leu	Ala	Cys	Ile	Lys	Leu	Gly	Ser	Glu	Asp	Lys	
		95					100					105					
15														GTT			447
		Leu	Gly	Arg	Leu		His	Cys	Pro	Ile		Thr	Gln	Val	Leu		
	110					115					120					125	
														CAG			495
•	Glu	Ala	Glu	Glu		Gln	Glu	Thr	Gln	•	Leu	Arg	Val	Gln		Ala	
20					130					135					140	m 00	5 4.0
														GCC			543
	GIA	GIU	Asp		HIS	Ser	Pne	Tyr		Pro	GIY	GIN	Pne	Ala	Pne	ser	
	A A C	ccc	CTC	145	ccc	۸۵۵	ጥል ልረ	20040	150	~ m C A (· cmc (ים שנ	ירייירי	155			590
25							IAA	GCCAC	JCA (TGAC	-6160	.G 10	.6160	,616			290
2.,	Lys	VIG	160	Pro	urg	261											
	CAGO	ACC		cece	277667	ΓΔ Δ /	יר ג בי	rcc A /	CA(ccc	AGCC	ccci	vece.	AGA (CACC	CCCGTT	650
								rgct(ion (onoc	200011	695
	01111	. 000	J110 V	JOMIC	min	11 111	moo.	10010	, 100	JONG	7160	010					0,5
30																	
	(2)	INFO	ORMA'	noi	FOR	SEO	ID 1	10: 5	54:								
	. ,							RIST									•
		•	•	-	LENG												
								ic ac	cid								
35								S: Do		•							
				(D)	TOPO	LOGY	: Li	inear	•						•	•	

(ii) SEQUENCE KIND: cDNA to mRNA

WO 98/55508

		(v	1) 0	KIGI	TAVE	SOUR	CE:				-						
				(A)	ORGA	MISH	i: Ho	omo s	sapie	ens							
	(B) CELL KIND: Stomach cancer																
	(D) CLONE NAME: HP10480																
5																	
		(i	.x) S	EQUE	ENCE	CHAR	ACTI	ERIST	CICS	:							
	(A) CHARACTERIZATION CODE: CDS																
				(B)	EXIS	STENC	E PO	SIT	ON:	80	661	L					
				(C)	CHA	RACTE	ERIZA	ATIO	ME	HOD:	E					•	
10																	
		(x	i) S	EQUE	ENCE	DESC	CRIPT	NOI	: SEC) ID	NO:	54:					
																CTCGG	
	CCC	CGCGC	CCG C	CCG	PCAA(TGC	112
15								e Ar	g Cys			ı Ala	a Cys	s Glu		g Cys	
]	-							mmo	10		160
		TGG															100
	Arg	Trp	Ile		Pro	Leu	Leu	Leu		Ser	Ala	TIE	Ala	25	Asp	TIE	
00		GCG	0.00	15	000	000	000	maa	20	C 4 C	mcm	A.C.C	CAC		ccc	CAG	208
20		Ala															200
	116	ALA	30	ALG	Gly	urg	Gly	35	Deu	GIII	361	561	40		0		
	ACG	TCC		стс	ፕርር	TGG	AAA		TCC	CAA	GAG	GGC		GGC	AGC	GGG	256
		Ser															
25		45					50	-,-				55	•	·			
	TCC	TAC	GAG	GAG	GGC	TGT	CAG	AGC	CTC	ATG	GAG	TAC	GCG	TGG	GGT	AGA	304
		Tyr															
	60					65					70					75	
	GCA	GCG	GCT	GCC	ATG	CTC	TTC	TGT	GGC	TTC	ATC	ATC	CTG	GTG	ATC	TGT	352
30	Ala	Ala	Ala	Ala	Met	Leu	Phe	Cys	Gly	Phe	Ile	Ile	Leu	Va1	Ile	Cys	
					80					85					90		
	TTC	ATC	CTC	TCC	TTC	TTC	GCC	CTC	TGT	GGA	CCC	CAG	ATG	CTT	GTC	TTC	400
	Phe	Ile	Leu	Ser	Phe	Phe	Ala	Leu	Cys	Gly	Pro	Gln	Met	Leu	Val	Phe	
				95					100					105			
35	CTG	AGA	GTG	ATT	GGA	GĢT	CTC	CTT	GCC	TTG	GCT	GÇT	GTG	TTC	CAG	ATC	448
	Leu	Arg	Val	Ile	Gly	Gly	Leu	Leu	Ala	Leu	Ala	Ala	Val	Phe	Gln	Ile	
			110					115					120			•	
	ATC	TCC	CTG	GTA	ATT	TAC	CCC	GTG	AAG	TAC	ACC	CAG	ACC	TTC	ACC	CTT	496

	Ile	Ser	Leu	Val	Ile	Tyr	Pro	Val	Lys	Tyr	Thr	Gln	Thr	Phe	Thr	Leu	
		125					130					135					
	CAT	GCC	AAC	CGT	GCT	GTC	ACT	TAC	ATC	TAT	AAC	TGG	GCC	TAC	GGC	TTT	544
	His	Ala	Asn	Arg	Ala	Val	Thr	Tyr	Ile	Tyr	Asn	Trp	Ala	Tyr	Gly	Phe	
5	140					145					150					155	
	GGG	TGG	GCA	GCC	ACG	ATT	ATC	CTG	ATC	GGC	TGT	GCC	TTC	TTC	TTC	TGC	592
	Gly	Trp	Ala	Ala	Thr	Ile	Ile	Leu	Ile	Gly	Cys	Ala	Phe	Phe	Phe	Cys	
					160					165					170		
	TGC	CTC	CCC	AAC	TAC	GAA	GAT	GAC	CTT	CTG	GGC	AAT	GCC	AAG	CCC	AGG	640
10	Cys	Leu	Pro	Asn	Tyr	Glu	Asp	Asp	Leu	Leu	Gly	Asn	Ala	Lys	Pro	Arg	
				175					180					185			
	TAC	TTC	TAC	ACA	TCT	GCC	TA A	ACTTO	GG A	AATG	AATG	rg go	GAGA	AAT	C GC	r	690
	Tyr	Phe	Tyr	Thr	Ser	Ala											
			190														
15	GCTG	CTGA	AGA '	TGGA	CTCCA	AG A	AGAA	GAAAC	TG!	rttci	CCA	GGC	GACTI	TTG A	AACC	CATTT	750
	TTGG	CAG	rgt '	TCATA	ATTA	A TI	AACT	AGTC	A AA	AATG	CTAA	AATA	ATTI	rgg (GAGA	AAAFA?	r 810
	TTTT	TAAC	GTA (GTGT	ATAT	T T	CAT	GTTT#	A TC	rttt/	ATTA	TGT'	rttgi	rga A	AGTTO	STGTCT	r 870
	TTTC	CACTA	'TAA	TACC	OATAT	CT A	rgcc	AATA	TT(CCTTA	TAT	CTA:	CCA	AA'	CATT	CATAC	r 930
	ACAT	TTG	CAA (GAGA	TAT	C A	CGTG	AAACI	AT 7	ACACI	ATTT	TAAC	GTA	AAA A	ATGAC	GTTTC	990
20	CAAG	ATTI	'AA	TAATO	CTGAT	C A	AGTT(CTTGI	TA!	rttco	CAAA	TAG	AATGG	AC 1	rtgg	CTGT	1050
	AAGG	GCTA	AAG (GAGA/	AGAGO	A A	ATA	AGGTT	AAA 7	AAGTT	GTT	AATO	SACCA	AA (CATTO	TAAAA	1110
	GAAA	TGCA	AAA	AAAA	AAGTI	T A	TTTT	CAAGO	CT	rcga/	ACTA	TTT	AGGA	AA (GCAAA	AATCA	1170
	TTCC	TAAA	ATG (CATA	CAT	TT G	rgag <i>i</i>	AATTI	CTO	CATTA	ATA	TCC	rgaa'i	CA!	rtca:	TTCAG	1230
	CTAA	.GGC1	TC .	ATGT	rgac?	C G	TAT	GTCAT	CTA	AGGAA	AAGT	ACTA	ATTTC	CAT	GGTC	CAAACO	1290
25	TGTT	GCCA	ATA (GTTG	CAATE	G C	TTTC	CTTTA	A AG	TGTG!	TAAA	ATT:	ragai	GA A	AATTI	TCTCT	1350
	TTTA	LAAGI	TTC '	TTTA	raggo	T T	AGGG'	TGTGC	G GA	AAATO	CTA	TAT	TAATA	AA.	rctgi	ragtgi	1410
	TTTG	TGT	TA '	TATG	TTCAC	A A	CCAG	AGTAC	AC:	rggat	TGA	AAGA	ATGGA	CT (GGT	TAAT	1470
	TATO	ATGA	ACT (GATAC	GATC	rg g)AAT1	GTTGT	GTA	AGTA/	AAGC	ATTA	AGGAG	GG :	CAT	CTTGT	1530
	CACA	AAA	STG (CCAC	AAA 1	C A	CCT	CAGGA	A GA	ATAAA	ATGA	CTT	CTTI	TC :	'AAA'	CTCAC	1590
30	GTTT	ATCI	rgg (GCTCT	ratc <i>i</i>	AT A	raga(CAGG	C TTC	CTGAT	TAGT	TTG	CAACI	GT A	AAGCA	AGAAAC	1650
	CTAC	ATA	CAG '	TTAA.	AATC	T G	TCT'	TTCTI	r GG:	TAAAC	CAGA	TTT	[AAA]	GT (CTGAT	AAATAT	1710
	ACAT	GCCA	ACA (GGAGA	ATTO	CG G	GAT'	TTGAG	TT	rcrci	rgaa	TAG	CATAI	AT A	ATGAT	CCATO	1770
	GGAT	AGG	CA '	TTATO	ATT	T T	racc.	ATTTC	GAG	CTTAC	CATA	ATG	AAAA	CA A	ATTCA	ATTTT#	1830
	AATA	TCAC	AT '	TATTA	ATTTI	CG T	AGT'	TGTGG	AAA	AAAG	CTAA	TTG	ragti	TT (CATTA	TGAA	1890
35	TTTT	CCCA	AAT A	AAAC	CAGG	'A T'	гст										1914

157

CLAIMS

- A protein comprising an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ
 ID NOS: 1 to 18.
 - 2. A DNA encoding the protein according to claim 1.
- 3. A cDNA comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.
 - 4. A cDNA according to claim 3, which comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.
 - 5. An expression vector capable of in vitro translating the DNA according to any of claims 2 to 4 or expressing said DNA in an eukaryotic cell.

20

15

6. A transformed eukaryotic cell capable of expressing the DNA according to any of claims 2 to 4 to produce the protein according to claim 1.

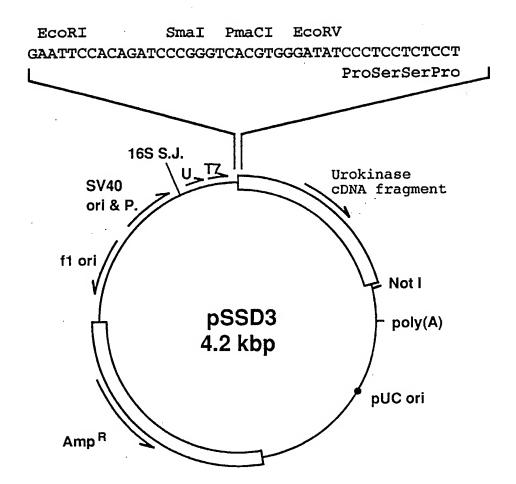


Fig.1

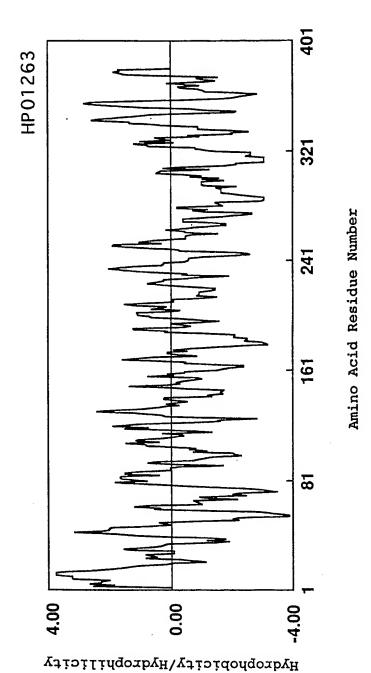
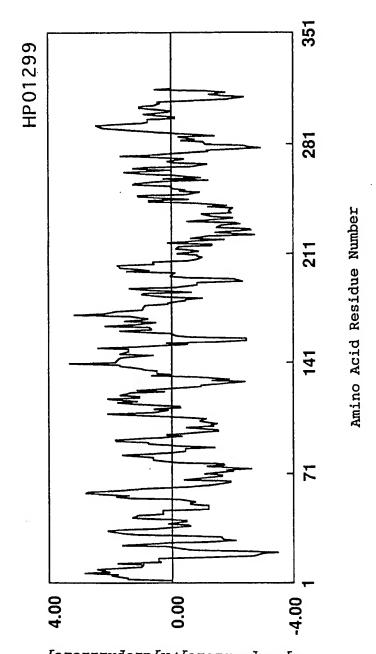


Fig.2



 ${\tt H} \lambda {\tt q} {\tt x} {\tt o} {\tt b} {\tt y} {\tt o} {\tt p} {\tt f} {\tt c} {\tt f} {\tt A} {\tt d} {\tt x} {\tt q} {\tt x} {\tt o} {\tt b} {\tt y} {\tt f} {\tt f} {\tt c} {\tt f} {\tt A}$

Fig.3

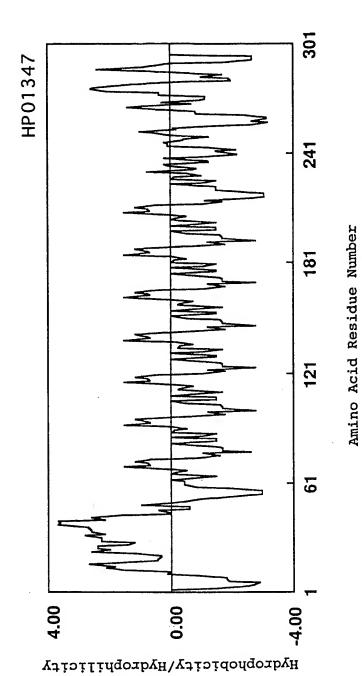


Fig.4

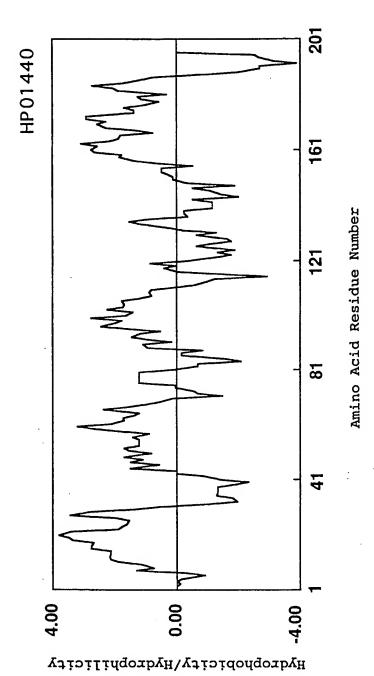


Fig.5

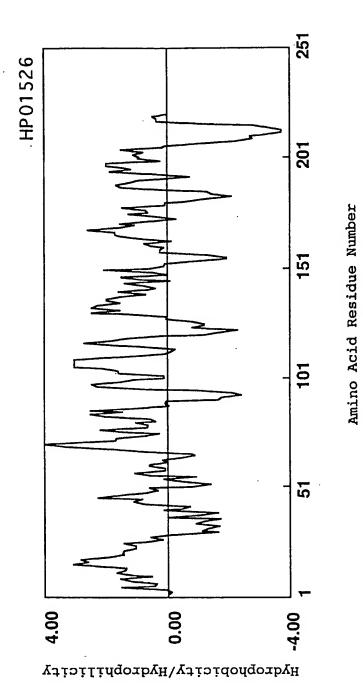


Fig.6

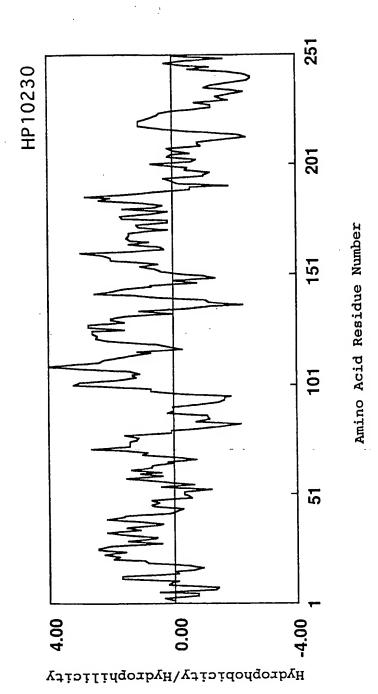


Fig.7

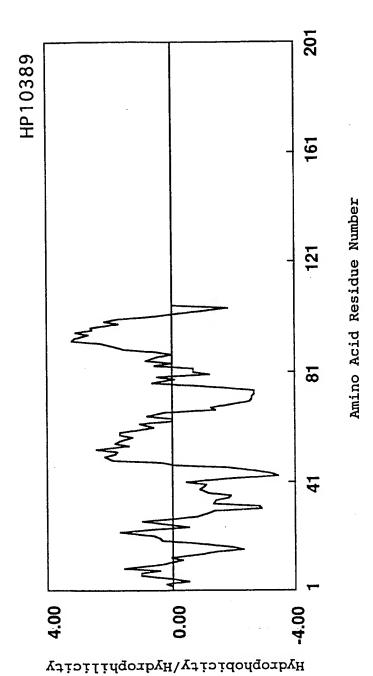


Fig.8

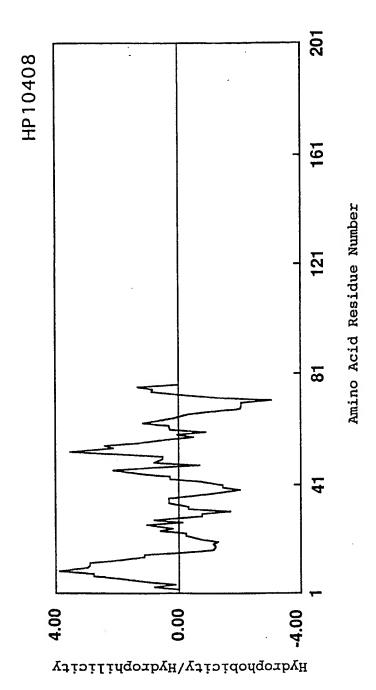


Fig.9

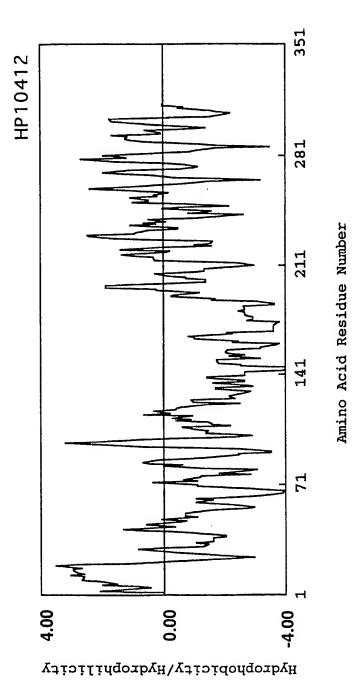


Fig.10

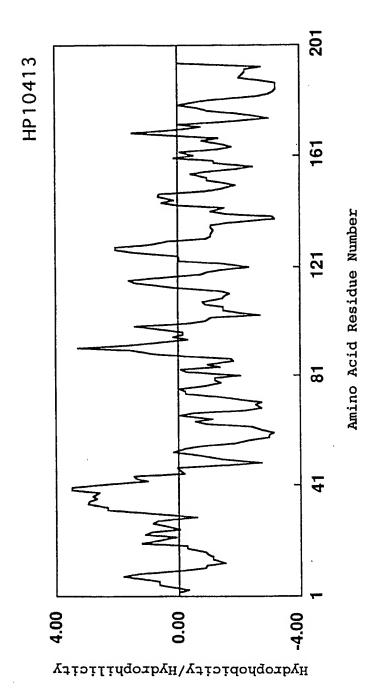
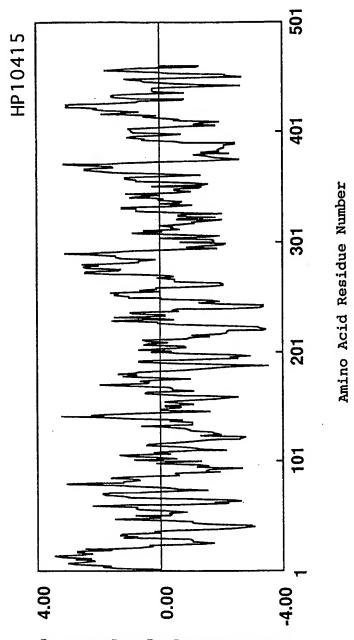


Fig.11



 ${\tt H} \lambda {\tt q} {\tt xobyop;c;f} \lambda \backslash {\tt H} \lambda {\tt q} {\tt xobyij;c;f} \lambda$

Fig.12

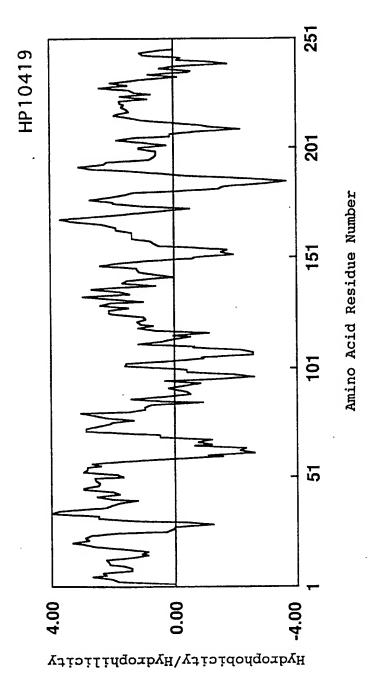


Fig.13

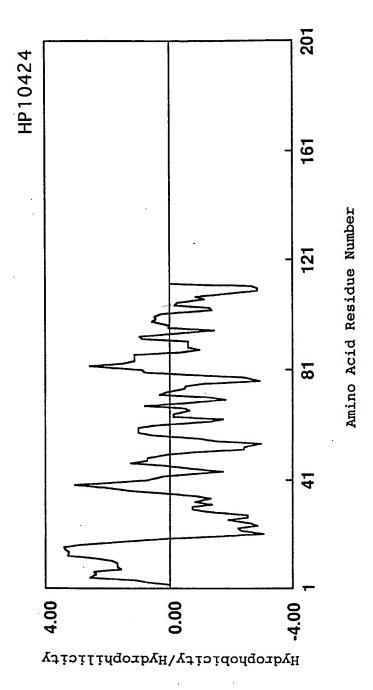
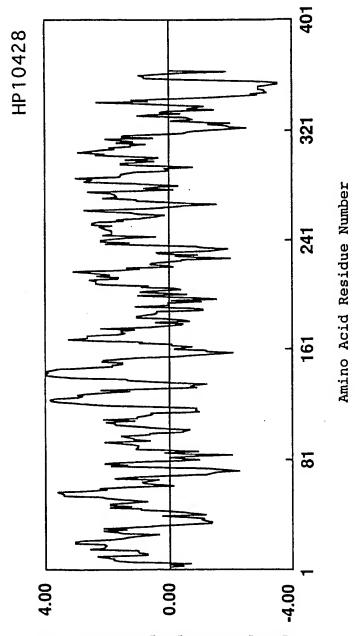


Fig.14



 ${\tt H} \lambda {\tt q} {\tt x} {\tt ob} {\tt y} {\tt op} {\tt i} {\tt c} {\tt i} {\tt c} {\tt h} {\tt A} {\tt q} {\tt x} {\tt ob} {\tt y} {\tt i} {\tt f} {\tt c} {\tt i} {\tt c} {\tt h}$

Fig.15

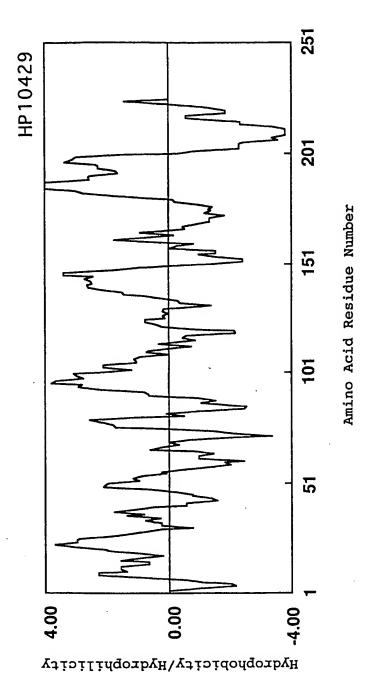


Fig.16

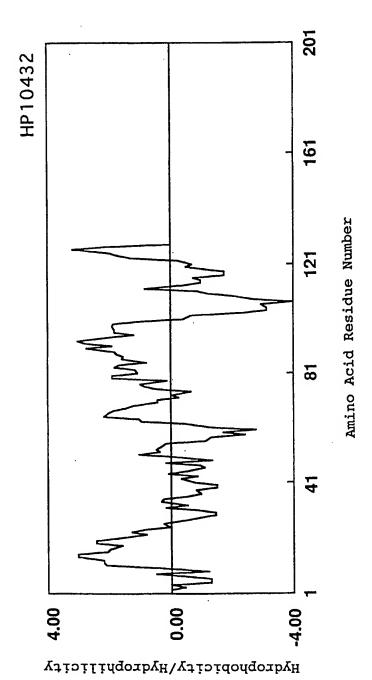


Fig.17

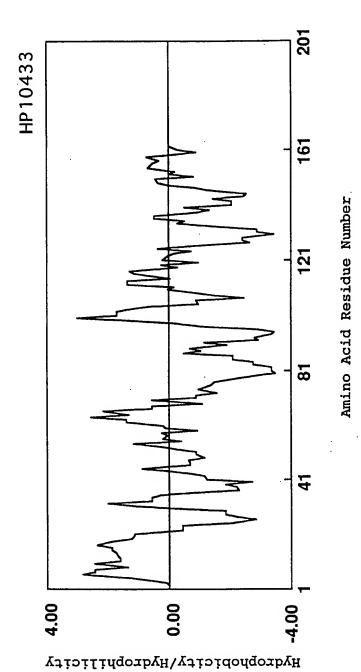


Fig.18

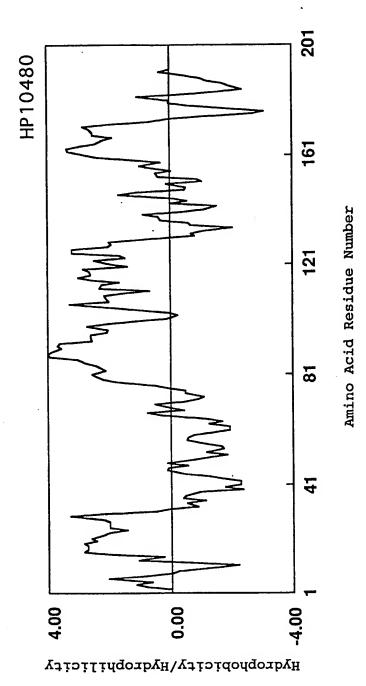


Fig.19